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=> S (Endou, Hitoshi)/au OR (Kanai, Yoshikatsu)/au OR (Johnson, Richard)/au OR
(Price, Karen)/au
L1 1919 (ENDOU, HITOSHI)/AU OR (KANAI, YOSHIKATSU)/AU OR (JOHNSON, RICHARD)/AU OR (PRICE, KAREN)/AU

=> S L1 AND URAT1
L2 108 L1 AND URAT1

=> Dup Rem L2
PROCESSING COMPLETED FOR L2
L3 53 DUP REM L2 (55 DUPLICATES REMOVED)
ANSWERS '1-22' FROM FILE MEDLINE
ANSWERS '23-40' FROM FILE BIOSIS
ANSWERS '41-53' FROM FILE CAPLUS

=> D Ibib abs L3 1-53

L3	ANSWER 1 OF 53	MEDLINE on STN	DUPLICATE 1
ACCESSION NUMBER:	2010931378	MEDLINE	
DOCUMENT NUMBER:	PubMed ID: 20810651		
TITLE:	Human sodium phosphate transporter 4 (hNPT4/SLC17A3) as a common renal secretory pathway for drugs and urate.		
AUTHOR:	Jutabha Promsuk; Anzai Naohiko; Kitamura Kenichiro; Taniguchi Atsuo; Kaneko Shuji; Yan Kunimasa; Yamada Hideomi; Shimada Hidetaka; Kimura Toru; Katada Tomohisa; Fukutomi Toshiyuki; Tomita Kimio; Urano Wako; Yamanaka Hisashi; Seki George; Fujita Toshiro; Moriyama Yoshinori; Yamada Akira; Uchida Shunya; Wempe Michael F; Endou Hitoshi; Sakurai Hiroyuki		
CORPORATE SOURCE:	Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo 181-8611, Japan.		
SOURCE:	The Journal of biological chemistry, (2010 Nov 5) Vol. 285, No. 45, pp. 35123-32. Electronic Publication: 2010-09-01. Journal code: 2985121R. E-ISSN: 1083-351X. L-ISSN:		

0021-9258.

Report No.: NLM-PMC2966126 [Available on 11/05/11].

United States

PUB. COUNTRY:
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 201011

ENTRY DATE: Entered STN: 2 Nov 2010

Last Updated on STN: 17 Dec 2010

Entered Medline: 30 Nov 2010

AB The evolutionary loss of hepatic urate oxidase (uricase) has resulted in humans with elevated serum uric acid (urate). Uricase loss may have been beneficial to early primate survival. However, an elevated serum urate has predisposed man to hyperuricemia, a metabolic disturbance leading to gout, hypertension, and various cardiovascular diseases. Human serum urate levels are largely determined by urate reabsorption and secretion in the kidney. Renal urate reabsorption is controlled via two proximal tubular urate transporters: apical URAT1 (SLC22A12) and basolateral URATv1/GLUT9 (SLC2A9). In contrast, the molecular mechanism(s) for renal urate secretion remain unknown. In this report, we demonstrate that an orphan transporter hNPT4 (human sodium phosphate transporter 4; SLC17A3) was a multispecific organic anion efflux transporter expressed in the kidneys and liver. hNPT4 was localized at the apical side of renal tubules and functioned as a voltage-driven urate transporter. Furthermore, loop diuretics, such as furosemide and bumetanide, substantially interacted with hNPT4. Thus, this protein is likely to act as a common secretion route for both drugs and may play an important role in diuretics-induced hyperuricemia. The in vivo role of hNPT4 was suggested by two hyperuricemia patients with missense mutations in SLC17A3. These mutated versions of hNPT4 exhibited reduced urate efflux when they were expressed in *Xenopus* oocytes. Our findings will complete a model of urate secretion in the renal tubular cell, where intracellular urate taken up via OAT1 and/or OAT3 from the blood exits from the cell into the lumen via hNPT4.

L3 ANSWER 2 OF 53

MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 2010516828 MEDLINE

DOCUMENT NUMBER: PubMed ID: 20560471

TITLE: Human renal urate transporter URAT1 mediates the transport of salicylate.

AUTHOR: Ohtsu Naoko; Anzai Naohiko; Fukutomi Toshiyuki; Kimura Toru; Sakurai Hiroyuki; Endou Hitoshi

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo, Japan.

SOURCE: Nippon Jinzo Gakkai shi, (2010) Vol. 52, No. 4, pp. 499-504.

Journal code: 7505731. ISSN: 0385-2385. L-ISSN: 0385-2385.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 201008

ENTRY DATE: Entered STN: 22 Jun 2010

Last Updated on STN: 4 Aug 2010

Entered Medline: 3 Aug 2010

AB Salicylic acid derivatives are the most prescribed analgesic-antipyretic and anti-inflammatory agents. It is well known that salicylate has a paradoxical effect on renal urate excretion. At low doses (5 - 10 mg/dL serum), renal urate excretion is decreased, whereas at high doses (> 15

mg/dL serum), renal urate excretion is increased. Since the molecular identification of the renal apical urate/anion exchanger URAT1, it has been suggested that this protein is responsible for the paradoxical effect because of cis-inhibition of salicylate (1 mM) on urate uptake by URAT1-expressing oocytes. The purpose of this study was to examine whether or not URAT1 is responsible for the paradoxical effect of salicylate. In URAT1-stably expressing HEK293 (HEK293-URAT1) cells, salicylate inhibited [¹⁴C] urate uptake dose-dependently (IC₅₀, 23.9 μM). URAT1 mediated the time-dependent uptake of [³H] salicylate in these cells. [³H] Salicylate uptake via URAT1 was inhibited by non-labelled urate and salicylate, and the uricosuric agent, benzbromarone. In the URAT1-expressing oocytes, we observed the time- and concentration-dependent transport of salicylate (K_m : 25.3 μM). Moreover, non-labelled salicylate injected into the URAT1-expressing oocytes stimulated [¹⁴C] urate uptake. These results suggest that the "paradoxical effect" of salicylate can be explained by two modes of salicylate interaction with URAT1 : (1) acting as an exchange substrate to facilitate urate reabsorption, and (2) acting as an inhibitor for urate reabsorption.

L3 ANSWER 3 OF 53 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 2010026529 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 20075570
 TITLE: Effect of fenofibrate on uric acid metabolism and urate transporter 1.
 AUTHOR: Uetake Daijiro; Ohno Iwao; Ichida Kimiyoshi; Yamaguchi Yuichiro; Saikawa Hajime; Endou Hitoshi; Hosoya Tatsuo
 CORPORATE SOURCE: Division of Kidney and Hypertension, Department of Internal Medicine, Jikei University School of Medicine, Tokyo. uetake@jikei.ac.jp
 SOURCE: Internal medicine (Tokyo, Japan), (2010) Vol. 49, No. 2, pp. 89-94. Electronic Publication: 2010-01-15. Journal code: 9204241. E-ISSN: 1349-7235. L-ISSN: 0918-2918.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: (COMPARATIVE STUDY)
 Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 201008
 ENTRY DATE: Entered STN: 16 Jan 2010
 Last Updated on STN: 8 Aug 2010
 Entered Medline: 6 Aug 2010
 AB OBJECTIVE: To examine the effects of fenofibrate, an antilipotropic drug, on uric acid metabolism in healthy male subjects and on urate transporter 1 (URAT1).
 METHODS: Fenofibrate was administered to nine male volunteers at a dose of 300 mg (corresponding to 200 mg of micronized fenofibrate), and the metabolic parameters of uric acid were investigated for more than 12 hours. In addition, the effect of fenofibrate on URAT1-expressing cells was examined.
 RESULTS: After the administration of fenofibrate, the concentration of serum uric acid had significantly decreased from 5.8±/−0.4 mg/dL to 4.3±/−0.3 mg/dL at 10 h. Uric acid clearance and the fractional excretion of uric acid increased. Fenofibric acid, a fenofibrate metabolite, inhibited URAT1 to an extent similar to that observed with benzbromarone and losartan.

CONCLUSION: Fenofibrate decreased serum uric acid levels by increasing its urinary excretion, most likely through the inhibition of URAT1 by fenofibric acid, its major metabolite.

L3 ANSWER 4 OF 53 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2008629342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18701466
TITLE: Plasma urate level is directly regulated by a voltage-driven urate efflux transporter URATv1 (SLC2A9) in humans.
AUTHOR: Anzai Naohiko; Ichida Kimiyoshi; Jutabha Promsuk; Kimura Toru; Babu Ellappan; Jin Chun Ji; Srivastava Sunena; Kitamura Kenichiro; Hisatome Ichiro; Endou Hitoshi; Sakurai Hiroyuki
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, 181-8611 Tokyo, Japan. anzai@ks.kyorin-u.ac.jp
SOURCE: The Journal of biological chemistry, (2008 Oct 3) Vol. 283, No. 40, pp. 26834-8. Electronic Publication: 2008-08-13. Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258. United States
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200811
ENTRY DATE: Entered STN: 1 Oct 2008
Last Updated on STN: 5 Nov 2008
Entered Medline: 4 Nov 2008

OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record
AB Hyperuricemia is a significant factor in a variety of diseases, including gout and cardiovascular diseases. Although renal excretion largely determines plasma urate concentration, the molecular mechanism of renal urate handling remains elusive. Previously, we identified a major urate reabsorptive transporter, URAT1 (SLC22A12), on the apical side of the renal proximal tubular cells. However, it is not known how urate taken up by URAT1 exits from the tubular cell to the systemic circulation. Here, we report that a sugar transport facilitator family member protein GLUT9 (SLC2A9) functions as an efflux transporter of urate from the tubular cell. GLUT9-expressed *Xenopus* oocytes mediated saturable urate transport (K_m : 365 \pm 42 μ M). The transport was Na(+)-independent and enhanced at high concentrations of extracellular potassium favoring negative to positive potential direction. Substrate specificity and pyrazinoate sensitivity of GLUT9 was distinct from those of URAT1. The in vivo role of GLUT9 is supported by the fact that a renal hypouricemia patient without any mutations in SLC22A12 was found to have a missense mutation in SLC2A9, which reduced urate transport activity in vitro. Based on these data, we propose a novel model of transcellular urate transport in the kidney; urate [corrected] is taken up via apically located URAT1 and exits the cell via basolaterally located GLUT9, which we suggest be renamed URATv1 (voltage-driven urate transporter 1).

L3 ANSWER 5 OF 53 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2008796217 MEDLINE
DOCUMENT NUMBER: PubMed ID: 19026395
TITLE: Mutations in glucose transporter 9 gene SLC2A9 cause renal hypouricemia.
AUTHOR: Matsuo Hirotaka; Chiba Toshinori; Nagamori Shushi; Nakayama Akiyoshi; Kimoto Hideharu; Phetdee Kanokporn; Wiriyasernkul Pattama; Dokuchi Yuichi; Oda Takashi; Nishiyama Junichiro; Nakamura Takahiro; Morimoto Yuji; Kamakura Keiko; Sakurai

Yutaka; Nonoyama Shigeaki; Kanai Yoshikatsu;
Shinomiya Nariyoshi
CORPORATE SOURCE: Department of Integrative Physiology and Bio-Nano Medicine,
National Defense Medical College, Tokorozawa, Saitama,
Japan. hmatsuo@ndmc.ac.jp
SOURCE: American journal of human genetics, (2008 Dec) Vol. 83, No.
6, pp. 744-51. Electronic Publication: 2008-11-20.
Journal code: 0370475. E-ISSN: 1537-6605. L-ISSN:
0002-9297.
Report No.: NLM-PMC2668068.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-BC018897; GENBANK-BC110414
ENTRY MONTH: 200901
ENTRY DATE: Entered STN: 11 Dec 2008
Last Updated on STN: 7 Jan 2009
Entered Medline: 6 Jan 2009

OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record
MEDLINE REFERENCE COUNT: 27 There are 27 cited references available in
MEDLINE for this document.

AB Renal hypouricemia is an inherited disorder characterized by impaired
renal urate (uric acid) reabsorption and subsequent low serum urate
levels, with severe complications such as exercise-induced acute renal
failure and nephrolithiasis. We previously identified SLC22A12, also
known as URAT1, as a causative gene of renal hypouricemia.
However, hypouricemic patients without URAT1 mutations, as well
as genome-wide association studies between urate and SLC2A9 (also called
GLUT9), imply that GLUT9 could be another causative gene of renal
hypouricemia. With a large human database, we identified two
loss-of-function heterozygous mutations in GLUT9, which occur in the
highly conserved "sugar transport proteins signatures 1/2." Both mutations
result in loss of positive charges, one of which is reported to be an
important membrane topology determinant. The oocyte expression study
revealed that both GLUT9 isoforms showed high urate transport activities,
whereas the mutated GLUT9 isoforms markedly reduced them. Our findings,
together with previous reports on GLUT9 localization, suggest that these
GLUT9 mutations cause renal hypouricemia by their decreased urate
reabsorption on both sides of the renal proximal tubules. These findings
also enable us to propose a physiological model of the renal urate
reabsorption in which GLUT9 regulates serum urate levels in humans and can
be a promising therapeutic target for gout and related cardiovascular
diseases.

L3 ANSWER 6 OF 53 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2008249567 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18409511
TITLE: Molecular mechanisms of urate transport in renal tubules:
localization and function of urate transporters.
AUTHOR: Kanai Yoshikatsu
CORPORATE SOURCE: Division of Bio-system Pharmacology, Department of
Pharmacology, Graduate School of Medicine, Osaka
University.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2008
Apr) Vol. 66, No. 4, pp. 659-66. Ref: 20
Journal code: 0420546. ISSN: 0047-1852. L-ISSN: 0047-1852.
Japan
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200805
ENTRY DATE: Entered STN: 16 Apr 2008
Last Updated on STN: 31 May 2008
Entered Medline: 30 May 2008

REFERENCE COUNT: 20 There are 20 cited references for this document.

AB Urate, a naturally occurring product of purine metabolism, is present at higher levels in human blood than in other mammals, because humans have an effective renal urate reabsorption system in addition to their evolutionary loss of hepatic uricase by mutational silencing. The urate transporter URAT1 encoded by SLC22A12 is a urate anion exchanger regulating blood urate levels. URAT1 is localized in the apical membrane of renal proximal tubules and targeted by uricosuric and antiuricosuric agents. Idiopathic renal hypouricemia is due to the genetic defect of SLC22A12. Recently it has been shown that the proximal tubule apical membrane organic anion transporter OAT4 transports urate at low affinity and responsible for the hyperuricemia caused by thiazide diuretics. Transport of urate via URAT1 is driven by the intracellular lactate that is accumulated by Na⁺/lactate cotransporter slc5a8 and slc5a12. URAT1 is proposed to be involved in the multimolecular complex "transportsome" that allows the cooperation of multiple transporters.

L3 ANSWER 7 OF 53 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2008430048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18600508
TITLE: Urate transport across the apical membrane of renal proximal tubules.
AUTHOR: Endou Hitoshi; Anzai Naohiko
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo, Japan.
endouh@kyorin-u.ac.jp
SOURCE: Nucleosides, nucleotides & nucleic acids, (2008 Jun) Vol. 27, No. 6, pp. 578-84.
Journal code: 100892832. E-ISSN: 1532-2335. L-ISSN: 1525-7770.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200810
ENTRY DATE: Entered STN: 8 Jul 2008
Last Updated on STN: 31 Oct 2008
Entered Medline: 30 Oct 2008

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB Since the molecular cloning of the renal apical urate/anion exchanger URAT1 (SLC22A12), several membrane proteins relevant to urate transport have been identified. In addition, the identification of PDZ (PSD-95, Dgla, and ZO-1) domain protein PDZK1 as a binding partner of URAT1, and the emerging role of PDZ scaffold for renal apical transporters have led to a new concept of renal urate transport: urate-transporting multimolecular complex, or "urate transportsome," that may form an ultimate functional unit at the apical membrane of renal proximal tubules. Elucidation of urate transportsome will lead to the new drug development for hyperuricemia.

L3 ANSWER 8 OF 53 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2007079906 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17278930

TITLE: New insights into renal transport of urate.
 AUTHOR: Anzai Naohiko; Kanai Yoshikatsu; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Shinkawa, Mitaka-shi, Tokyo, Japan.
 SOURCE: Current opinion in rheumatology, (2007 Mar) Vol. 19, No. 2, pp. 151-7. Ref: 72
 Journal code: 9000851. ISSN: 1040-8711. L-ISSN: 1040-8711.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200703
 ENTRY DATE: Entered STN: 7 Feb 2007
 Last Updated on STN: 30 Mar 2007
 Entered Medline: 29 Mar 2007
 OS.CITING REF COUNT: 11 There are 11 MEDLINE records that cite this record
 REFERENCE COUNT: 72 There are 72 cited references for this document.
 AB PURPOSE OF REVIEW: This review focuses on recent progress in the understanding of various aspects of renal transport of urate.

RECENT FINDINGS: Since the molecular cloning of the renal apical urate/anion exchanger URAT1 (SLC22A12), several membrane proteins relevant to the transport of urate have been identified. The molecular identification of two sodium-coupled monocarboxylate transporters, SMCT1 (SLC5A8) and SMCT2 (SLC5A12), and the emerging role of PDZ (PSD-95, Dgla, and ZO-1) scaffold for renal apical transporters have led to a new concept of renal urate transport: urate-transporting multimolecular complex, or 'urate transportosome', that may form an ultimate functional unit including the sodium-coupled urate transport system by linking URAT1 and sodium-coupled monocarboxylate transporters or the coordinated apical urate uptake system by balancing reabsorptive (URAT1) and efflux (NPT1/OATv1 and MRP4) transporters. In addition, genetic variations of the URAT1 gene are associated not only with idiopathic renal hypouricemia but also with reduced renal urate excretion.

SUMMARY: Although our knowledge of renal urate handling has been increased by the molecular identification of urate transport proteins and by results of genetic studies on patients with serum urate disorders, current evidence is insufficient to fully understand the precise mechanism governing the bi-directional transport of urate. Further studies are still necessary.

L3 ANSWER 9 OF 53 MEDLINE on STN DUPLICATE 12
 ACCESSION NUMBER: 2006381728 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 16775029
 TITLE: Human vascular smooth muscle cells express a urate transporter.
 AUTHOR: Price Karen L; Sautin Yuri Y; Long David A; Zhang Li; Miyazaki Hiroki; Mu Wei; Endou Hitoshi; Johnson Richard J
 CORPORATE SOURCE: Division of Nephrology, Hypertension, and Transplantation, University of Florida, Gainesville, Florida, USA.
 regnkpr@ucl.ac.uk
 CONTRACT NUMBER: DK-52121 (United States NIDDK NIH HHS)
 HL-68607 (United States NHLBI NIH HHS)
 KD-64233 (United States PHS HHS)
 SOURCE: Journal of the American Society of Nephrology : JASN, (2006

Jul) Vol. 17, No. 7, pp. 1791-5. Electronic Publication:
2006-06-14.

Journal code: 9013836. ISSN: 1046-6673. L-ISSN: 1046-6673.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200610

ENTRY DATE: Entered STN: 27 Jun 2006

Last Updated on STN: 31 Oct 2006

Entered Medline: 30 Oct 2006

OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record

AB An elevated serum uric acid is associated with the development of hypertension and renal disease. Renal regulation of urate excretion is largely controlled by URAT1 (SLC22A12), a member of the organic anion transporter superfamily. This study reports the specific expression of URAT1 on human aortic vascular smooth muscle cells, as assessed by reverse transcription-PCR and Western blot analysis. Expression of URAT1 was localized to the cell membrane. Evidence that the URAT1 transporter was functional was provided by the finding that uptake of 14C-urate was significantly inhibited in the presence of probenecid, an organic anion transporter inhibitor. It is proposed that URAT1 may provide a mechanism by which uric acid enters the human vascular smooth muscle cell, a finding that may be relevant to the role of uric acid in cardiovascular disease.

L3 ANSWER 10 OF 53

MEDLINE on STN

DUPLICATE 13

ACCESSION NUMBER: 2006382258 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16799257

TITLE: Organic anion transporter family: current knowledge.

AUTHOR: Anzai Naohiko; Kanai Yoshikatsu; Endou

Hitoshi

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin
University School of Medicine, Tokyo, Japan.

SOURCE: Journal of pharmacological sciences, (2006) Vol. 100, No.
5, pp. 411-26. Ref: 106

Journal code: 101167001. ISSN: 1347-8613. L-ISSN:
1347-8613.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200608

ENTRY DATE: Entered STN: 27 Jun 2006

Last Updated on STN: 26 Aug 2006

Entered Medline: 25 Aug 2006

OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record

REFERENCE COUNT: 106 There are 106 cited references for this document.

AB Organic anion transporters (OATs) play an essential role in the elimination of numerous endogenous and exogenous organic anions from the body. The renal OATs contribute to the excretion of many drugs and their metabolites that are important in clinical medicine. Several families of multispecific organic anion and cation transporters, including OAT family transporters, have recently been identified by molecular cloning. The OAT family consists of six isoforms (OAT1 - 4, URAT1, and rodent Oat5) and they are all expressed in the kidney, while some are also expressed in the liver, brain, and placenta. The OAT family represents mainly the renal secretory and reabsorptive pathway for organic anions and

is also involved in the distribution of organic anions in the body, drug-drug interactions, and toxicity of anionic substances such as nephrotoxic drugs and uremic toxins. In this review, current knowledge of and recent progress in the understanding of several aspects of OAT family members are discussed.

L3 ANSWER 11 OF 53 MEDLINE on STN DUPLICATE 14
 ACCESSION NUMBER: 2005276348 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15919000
 TITLE: Renal urate handling: clinical relevance of recent advances.
 AUTHOR: Anzai Naohiko; Enomoto Atsushi; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka-shi, Tokyo 181-8611, Japan. endouh@kyorin-u.ac.jp
 SOURCE: Current rheumatology reports, (2005 Jun) Vol. 7, No. 3, pp. 227-34. Ref: 50
 Journal code: 100888970. ISSN: 1523-3774. L-ISSN: 1523-3774.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200511
 ENTRY DATE: Entered STN: 28 May 2005
 Last Updated on STN: 15 Nov 2005
 Entered Medline: 14 Nov 2005
 OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
 REFERENCE COUNT: 50 There are 50 cited references for this document.
 AB Urate is the major inert end product of purine degradation in higher primates in contrast to most other mammals because of the genetic silencing of hepatic oxidative enzyme uricase. The kidney plays a dominant role in urate elimination. The kidney excretes 70% of the daily urate production. Therefore, it is important to understand renal urate handling mechanism because the under excretion of urate has been implicated in the development of hyperuricemia that leads to gout. The urate transport systems exist in the proximal tubule but they are complicated because of their bidirectional transport and the species differences. Recently, we have identified the urate-anion exchanger URAT1 (SLC22A12) in the human kidney and found that defects in SLC22A12 lead to idiopathic renal hypouricemia. URAT1 is targeted by uricosuric and antiuricosuric agents that affect urate excretion. Molecular identification of urate transporting proteins will lead to the new drug development for hyperuricemia.

L3 ANSWER 12 OF 53 MEDLINE on STN DUPLICATE 15
 ACCESSION NUMBER: 2005515467 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 16189627
 TITLE: Roles of organic anion transporters (OATs) and a urate transporter (URAT1) in the pathophysiology of human disease.
 AUTHOR: Enomoto Atsushi; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo, 181-8611, Japan.
 SOURCE: Clinical and experimental nephrology, (2005 Sep) Vol. 9, No. 3, pp. 195-205. Ref: 77
 Journal code: 9709923. ISSN: 1342-1751. L-ISSN: 1342-1751.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
English
LANGUAGE:
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 29 Sep 2005
Last Updated on STN: 24 Dec 2005
Entered Medline: 23 Dec 2005

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
REFERENCE COUNT: 77 There are 77 cited references for this document.

AB Renal proximal and distal tubules are highly polarized epithelial cells that carry out the specialized directional transport of various solutes. This renal function, which is essential for homeostasis in the body, is achieved through the close pairing of apical and basolateral carriers expressed in the renal epithelial cells. The family of organic anion transporters (OATs), which belong to the major facilitator superfamily (SLC22A), are expressed in the renal epithelial cells to regulate the excretion and reabsorption of endogenous and exogenous organic anions. We now understand that these OATs are crucial components in the renal handling of drugs and their metabolites, and they are implicated in various clinically important drug interactions, and their adverse reactions. In recent years, the molecular entities of these transporters have been identified, and their function and regulatory mechanisms have been partially clarified. Workers in this field have identified URAT1 (urate transporter 1), a novel member of the OAT family that displays unique and selective substrate specificity compared with other multispecific OATs. In the OAT family, URAT1 is the main transporter responsible for human genetic diseases. In this review, we introduce and discuss some novel aspects of OATs, with special emphasis on URAT1, in the context of their biological significance, functional regulation, and roles in human disease.

L3 ANSWER 13 OF 53 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 2005185528 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15772301
TITLE: Molecular physiology of urate transport.
AUTHOR: Hediger Matthias A; Johnson Richard J; Miyazaki Hiroki; Endou Hitoshi
CORPORATE SOURCE: Membrane Biology Program and Renal Division, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA. mhediger@rics.bwh.harvard.edu
SOURCE: Physiology (Bethesda, Md.), (2005 Apr) Vol. 20, pp. 125-33. Ref: 59
Journal code: 101208185. ISSN: 1548-9213. L-ISSN: 1548-9221.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 12 Apr 2005
Last Updated on STN: 16 Jul 2005
Entered Medline: 15 Jul 2005

OS.CITING REF COUNT: 11 There are 11 MEDLINE records that cite this record
REFERENCE COUNT: 59 There are 59 cited references for this document.

AB Humans excrete uric acid as the final breakdown product of unwanted purine nucleotides. Urate scavenges potential harmful radicals in our body. However, in conjunction with genetic or environmental (especially dietary) factors, urate may cause gout, nephrolithiasis, hypertension, and vascular disease. Blood levels of urate are maintained by the balance between generation and excretion. Excretion requires specialized transporters

located in renal proximal tubule cells, intestinal epithelial cells, and vascular smooth muscle cells. The recently identified human urate transporters URAT1, MRP4, OAT1, and OAT3 are thought to play central roles in homeostasis and may prove interesting targets for future drug development.

L3 ANSWER 14 OF 53 MEDLINE on STN DUPLICATE 17
 ACCESSION NUMBER: 2004552128 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15304510
 TITLE: The multivalent PDZ domain-containing protein PDZK1 regulates transport activity of renal urate-anion exchanger URAT1 via its C terminus.
 AUTHOR: Anzai Naohiko; Miyazaki Hiroki; Noshiro Rie; Khamdang Suparat; Chairoungdua Arthit; Shin Ho-Jung; Enomoto Atsushi; Sakamoto Shinichi; Hirata Taku; Tomita Kimio; Kanai Yoshikatsu; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka-shi, Tokyo 181-8611, Japan.
 SOURCE: The Journal of biological chemistry, (2004 Oct 29) Vol. 279, No. 44, pp. 45942-50. Electronic Publication: 2004-08-10.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200411
 ENTRY DATE: Entered STN: 5 Nov 2004
 Last Updated on STN: 19 Dec 2004
 Entered Medline: 30 Nov 2004

OS.CITING REF COUNT: 8 There are 8 MEDLINE records that cite this record
 AB The urate-anion exchanger URAT1 is a member of the organic anion transporter (OAT) family that regulates blood urate level in humans and is targeted by uricosuric and antiuricosuric agents. URAT1 is expressed only in the kidney, where it is thought to participate in tubular urate reabsorption. We found that the multivalent PDZ (PSD-95, Drosophila discs-large protein, Zonula occludens protein 1) domain-containing protein, PDZK1 interacts with URAT1 in a yeast two-hybrid screen. Such an interaction requires the PDZ motif of URAT1 in its extreme intracellular C-terminal region and the first, second, and fourth PDZ domains of PDZK1 as identified by yeast two-hybrid assay, in vitro binding assay and surface plasmon resonance analysis ($K_D = 1.97\text{--}514\text{ nM}$). Coimmunoprecipitation studies revealed that the wild-type URAT1, but not its mutant lacking the PDZ-motif, directly interacts with PDZK1. Colocalization of URAT1 and PDZK1 was observed at the apical membrane of renal proximal tubular cells. The association of URAT1 with PDZK1 enhanced urate transport activities in HEK293 cells (1.4-fold), and the deletion of the URAT1 C-terminal PDZ motif abolished this effect. The augmentation of the transport activity was accompanied by a significant increase in the V_{\max} of urate transport via URAT1 and was associated with the increased surface expression level of URAT1 protein from HEK293 cells stably expressing URAT1 transfected with PDZK1. Taken together, the present study indicates the novel role of PDZK1 in regulating the functional activity of URAT1-mediated urate transport in the apical membrane of renal proximal tubules.

L3 ANSWER 15 OF 53 MEDLINE on STN DUPLICATE 18
 ACCESSION NUMBER: 2004068771 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12883891

TITLE: The SLC22 drug transporter family.
 AUTHOR: Koepsell Hermann; Endou Hitoshi
 CORPORATE SOURCE: Institute of Anatomy and Cell Biology, Bayerische Maximilians Universität Würzburg, Koellikerstr. 6, 97070, Würzburg, Germany. Hermann@Koepsell.de
 SOURCE: Pflügers Archiv : European journal of physiology, (2004 Feb) Vol. 447, No. 5, pp. 666-76. Electronic Publication: 2003-07-19. Ref: 66
 Journal code: 0154720. ISSN: 0031-6768. L-ISSN: 0031-6768.
 PUB. COUNTRY: Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200409
 ENTRY DATE: Entered STN: 11 Feb 2004
 Last Updated on STN: 4 Sep 2004
 Entered Medline: 3 Sep 2004
 OS.CITING REF COUNT: 15 There are 15 MEDLINE records that cite this record
 REFERENCE COUNT: 66 There are 66 cited references for this document.
 AB The SLC22 family comprises organic cation transporters (OCTs), zwitterion/cation transporters (OCTNs), and organic anion transporters (OATs). These transporters contain 12 predicted alpha-helical transmembrane domains (TMDs) and one large extracellular loop between TMDs 1 and 2. Transporters of the SLC22 family function in different ways: (1) as uniporters that mediate facilitated diffusion in either direction (OCTs), (2) as anion exchangers (OAT1, OAT3 and URAT1), and (3) as Na(+)/ l-carnitine cotransporter (OCTN2). They participate in the absorption and/or excretion of drugs, xenobiotics, and endogenous compounds in intestine, liver and/or kidney, and perform homeostatic functions in brain and heart. The endogenous substrates include monoamine neurotransmitters, choline, l-carnitine, alpha-ketoglutarate, cAMP, cGMP, prostaglandins, and urate. Defect mutations of transporters of the SLC22 family may cause specific diseases such as "primary systemic carnitine deficiency" or "idiopathic renal hypouricemia" or change drug absorption or excretion.
 L3 ANSWER 16 OF 53 MEDLINE on STN DUPLICATE 19
 ACCESSION NUMBER: 2004046349 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14747372
 TITLE: Function and localization of urate transporter 1 in mouse kidney.
 AUTHOR: Hosoyamada Makoto; Ichida Kimiyoshi; Enomoto Atsushi; Hosoya Tatsuo; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo, Japan.
 hosoyamd@kyorin-u.ac.jp
 SOURCE: Journal of the American Society of Nephrology : JASN, (2004 Feb) Vol. 15, No. 2, pp. 261-8.
 Journal code: 9013836. ISSN: 1046-6673. L-ISSN: 1046-6673.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200409
 ENTRY DATE: Entered STN: 29 Jan 2004
 Last Updated on STN: 21 Sep 2004
 Entered Medline: 20 Sep 2004
 OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record
 AB Mouse renal-specific transporter (RST) cDNA, the amino acid sequence of which has 74% identity with that of human urate transporter 1 (hURAT1), is

potentially the mouse homologue of hURAT1, the gene responsible for hereditary renal hypouricemia. The aim of this study is to determine the location and characteristics of RST molecule in mouse kidney and investigate urate transport by RST using the *Xenopus* oocyte expression system. RST transported (14)C-urate in a Michaelis-Menten manner. The $K(m)$ and the $V(max)$ values of RST-dependent urate transport were 1213 +/- 222 micro M and 268.8 +/- 38.0 pmol/oocyte per hr, respectively (n = 3). RST-dependent urate transport was cis-inhibited significantly by 1 mM probenecid (68.7 +/- 9.4%), 50 micro M benzbromarone (67.9 +/- 6.4%), and 10 mM lactate (50.9 +/- 9.5%). However, 1 mM p-aminohippurate (PAH), 1 mM xanthine, and 1 mM oxonate did not inhibit RST-dependent urate transport. Substitution of Cl anion with gluconate in the external solution enhanced RST-dependent urate transport. Pre-injected pyrazinoic acid (PZA) or L-lactate trans-stimulated RST-dependent urate transport. Using immunohistochemistry for mouse kidney, the brush border or intracellular membrane of proximal tubules was stained by an affinity-purified antibody that recognized mouse URAT1 (mURAT1) expressed on *Xenopus* oocyte. Using Western blotting, anti-mURAT1 antibody detected 70-kD and 62-kD protein bands. The 70-kD protein was N-glycosylated and was identified as a Triton X-100 insoluble brush border membrane protein. RST mRNA and protein levels were higher in male kidneys than female. RST transported urate similar to hURAT1 and, therefore, appears to be mURAT1-the mouse homologue of hURAT1.

L3 ANSWER 17 OF 53 MEDLINE on STN DUPLICATE 20
 ACCESSION NUMBER: 2003610654 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14694169
 TITLE: Clinical and molecular analysis of patients with renal hypouricemia in Japan-influence of URAT1 gene on urinary urate excretion.
 AUTHOR: Ichida Kimiyoshi; Hosoyamada Makoto; Hisatome Ichiro; Enomoto Atsushi; Hikita Miho; Endou Hitoshi; Hosoya Tatsuo
 CORPORATE SOURCE: Division of Kidney and Hypertension, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan. ichida@jikei.ac.jp
 SOURCE: Journal of the American Society of Nephrology : JASN, (2004 Jan) Vol. 15, No. 1, pp. 164-73. Journal code: 9013836. ISSN: 1046-6673. L-ISSN: 1046-6673.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200405
 ENTRY DATE: Entered STN: 25 Dec 2003
 Last Updated on STN: 20 May 2004
 Entered Medline: 19 May 2004
 OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record
 AB Renal hypouricemia is an inherited and heterogeneous disorder characterized by increased urate clearance (CUA). The authors recently established that urate was reabsorbed via URAT1 on the tubular apical membrane and that mutations in SLC22A12 encoding URAT1 cause renal hypouricemia. This study was undertaken to elucidate and correlate clinical and genetic features of renal hypouricemia. The SLC22A12 gene was sequenced in 32 unrelated idiopathic renal hypouricemia patients, and the relationships of serum urate levels, and CUA/creatinine clearance (Ccr) to SLC22A12 genotype were examined. Uricosuric (probenecid and benzbromarone) and anti-uricosuric drug (pyrazinamide) loading tests were also performed in some patients. Three patients had exercise-induced acute renal failure (9.4%), and four patients had urolithiasis (12.5%). The authors identified eight new mutations and two

previously reported mutations that result in loss of function. Thirty patients had SLC22A12 mutations; 24 homozygotes and compound heterozygotes, and 6 heterozygotes. Mutation G774A dominated SLC22A12 mutations (74.1% in 54 alleles). Serum urate levels were significantly lower and CUA/Ccr was significantly higher in heterozygotes compared with healthy subjects; these changes were even more significant in homozygotes and compound heterozygotes. These CUA/Ccr relations demonstrated a gene dosage effect that corresponds with the difference in serum urate levels. In contrast to healthy subjects, the CUA/Ccr of patients with homozygous and compound heterozygous SLC22A12 mutations was unaffected by pyrazinamide, benzbromarone, and probenecid. The findings indicate that SLC22A12 was responsible for most renal hypouricemia and that URAT1 is the primary reabsorptive urate transporter, targeted by pyrazinamide, benzbromarone, and probenecid in vivo.

L3 ANSWER 18 OF 53 MEDLINE on STN DUPLICATE 21
 ACCESSION NUMBER: 2003574697 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14655203
 TITLE: Two male siblings with hereditary renal hypouricemia and exercise-induced ARF.
 AUTHOR: Tanaka Motoko; Itoh Kazuko; Matsushita Kazunori; Matsushita Kazutaka; Wakita Naoki; Adachi Masataka; Nonoguchi Hiroshi; Kitamura Kenichiro; Hosoyamada Makoto; Endou Hitoshi; Tomita Kimio
 CORPORATE SOURCE: Department of Nephrology, Akebono Clinic, Kumamoto, Japan. tanaka@matusita-kai.or.jp
 SOURCE: American journal of kidney diseases : the official journal of the National Kidney Foundation, (2003 Dec) Vol. 42, No. 6, pp. 1287-92.
 Journal code: 8110075. E-ISSN: 1523-6838. L-ISSN: 0272-6386.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CASE REPORTS)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200404
 ENTRY DATE: Entered STN: 16 Dec 2003
 Last Updated on STN: 23 Apr 2004
 Entered Medline: 22 Apr 2004

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
 AB Familial renal hypouricemia with exercise-induced acute renal failure (ARF) is rare. A 45-year-old man presented with abdominal pain, vomiting, and oliguria after severe exercise. The diagnosis was ARF based on high serum creatinine (Scr) level (5.1 mg/dL [451 micromol/L]). Renal function recovered completely within 2 weeks of conservative treatment (creatinine clearance [Ccr], 100.4 mL/min [1.67 mL/s]). After remission, laboratory results showed serum urate (SUA) of 0.8 mg/dL (48 micromol/L), and fractional excretion of uric acid (FE(UA)) of 46%. The final diagnosis was ARF associated with idiopathic renal hypouricemia. Other diseases that could increase the excretion of urate were excluded. Because only mild responses were observed both in pyrazinamide and benzbromarone loading tests, he was considered to be a presecretory reabsorption disorder type. The younger brother (42 years old) also had episodes of low and middle back pain after severe exercise and experienced similar attacks at least 5 times since the age of 29. Scr level was elevated in every attack. Hypouricemia (SUA, 1.0 mg/dL [59 micromol/L]) and high urinary urate excretion (FE(UA), 65.7%) also were detected. Renal function recovered almost completely without any specific treatment. Radiologic examination of the 2 cases showed bilateral urolithiasis probably caused by the high urinary urate excretion. Sequence analysis of a urate anion exchanger known to regulate blood urate level (URAT1

gene) in both brothers showed homozygous mutation in exon 4 (W258Stop), resulting in a premature truncated URAT1 protein. Both their parents and their children showed heterozygous mutation of the URAT1 gene. This is the first report of the 2 male siblings of familial renal hypouricemia complicated with exercise-induced ARF, with definite demonstration of genetic abnormality in the responsible gene (URAT1).

L3 ANSWER 19 OF 53 MEDLINE on STN DUPLICATE 22
 ACCESSION NUMBER: 2003482830 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14560659
 TITLE: Urate transporter and renal hypouricemia.
 AUTHOR: Enomoto Atsushi; Niwa Thosimitsu; Kanai Yoshikatsu
 ; Endou Hitoshi
 CORPORATE SOURCE: Nagoya University Hospital, Department of Clinical
 Preventive Medicine, Nagoya 466-8560.
 SOURCE: Rinsho byori. The Japanese journal of clinical pathology,
 (2003 Sep) Vol. 51, No. 9, pp. 892-7.
 Journal code: 2984781R. ISSN: 0047-1860. L-ISSN: 0047-1860.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200311
 ENTRY DATE: Entered STN: 17 Oct 2003
 Last Updated on STN: 13 Nov 2003
 Entered Medline: 12 Nov 2003

AB Urate, a purine metabolite, is a cause of gout(hyperuricemia), which is an independent risk factor for cardiovascular disease. Urate is a scavenger of reactive oxygen radicals that are involved in numerous diseases. Because humans have a renal urate reabsorption system and have lost hepatic uricase by mutational silencing in evolution, urate is present in human blood at high levels. We identified the long-hypothesized urate transporter in the human kidney (URAT1, encoded by SLC22A12), a urate anion exchanger regulating blood urate levels and targeted it with uricosuric and antiuricosuric agents. Moreover, we demonstrated that patients with renal hypouricemia have mutational defects in SLC22A12.

L3 ANSWER 20 OF 53 MEDLINE on STN DUPLICATE 23
 ACCESSION NUMBER: 2003094191 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12607260
 TITLE: Identification of a novel urate transporter URAT1
 and current status on urate research.
 AUTHOR: Endou Hitoshi; Miyazaki Hiroki; Anzai
 Naohikoendouh@kyorin-u.ac.jp
 SOURCE: Tanpakushitsu kakusan koso. Protein, nucleic acid, enzyme,
 (2003 Jan) Vol. 48, No. 1, pp. 18-25. Ref: 30
 Journal code: 0413762. ISSN: 0039-9450. L-ISSN: 0039-9450.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200304
 ENTRY DATE: Entered STN: 28 Feb 2003
 Last Updated on STN: 9 Apr 2003
 Entered Medline: 8 Apr 2003
 REFERENCE COUNT: 30 There are 30 cited references for this document.

L3 ANSWER 21 OF 53 MEDLINE on STN DUPLICATE 24
 ACCESSION NUMBER: 2002298327 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12024214
 TITLE: Molecular identification of a renal urate anion exchanger that regulates blood urate levels.
 AUTHOR: Enomoto Atsushi; Kimura Hiroaki; Chairoungdua Arthit; Shigeta Yasuhiro; Jutabha Promsuk; Cha Seok Ho; Hosoyamada Makoto; Takeda Michio; Sekine Takashi; Igarashi Takashi; Matsuo Hirotaka; Kikuchi Yuichi; Oda Takashi; Ichida Kimiyoshi; Hosoya Tatsuo; Shimokata Kaoru; Niwa Toshimitsu; Kanai Yoshikatsu; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo 181-8611, Japan.
 SOURCE: Nature, (2002 May 23) Vol. 417, No. 6887, pp. 447-52. Electronic Publication: 2002-04-14. Journal code: 0410462. ISSN: 0028-0836. L-ISSN: 0028-0836.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-AB071863; GENBANK-AC044790
 ENTRY MONTH: 200206
 ENTRY DATE: Entered STN: 2 Jun 2002
 Last Updated on STN: 19 Jun 2002
 Entered Medline: 18 Jun 2002

OS.CITING REF COUNT: 34 There are 34 MEDLINE records that cite this record
 AB Urate, a naturally occurring product of purine metabolism, is a scavenger of biological oxidants implicated in numerous disease processes, as demonstrated by its capacity of neuroprotection. It is present at higher levels in human blood (200 500 microM) than in other mammals, because humans have an effective renal urate reabsorption system, despite their evolutionary loss of hepatic uricase by mutational silencing. The molecular basis for urate handling in the human kidney remains unclear because of difficulties in understanding diverse urate transport systems and species differences. Here we identify the long-hypothesized urate transporter in the human kidney (URAT1, encoded by SLC22A12), a urate anion exchanger regulating blood urate levels and targeted by uricosuric and antiuricosuric agents (which affect excretion of uric acid). Moreover, we provide evidence that patients with idiopathic renal hypouricaemia (lack of blood uric acid) have defects in SLC22A12. Identification of URAT1 should provide insights into the nature of urate homeostasis, as well as lead to the development of better agents against hyperuricaemia, a disadvantage concomitant with human evolution.

L3 ANSWER 22 OF 53 MEDLINE on STN
 ACCESSION NUMBER: 2011149358 IN-PROCESS
 DOCUMENT NUMBER: PubMed ID: 21272127
 TITLE: Interactions of urate transporter URAT1 in human kidney with uricosuric drugs.
 AUTHOR: Shin Ho Jung; Takeda Michio; Enomoto Atsushi; Fujimura Masaaki; Miyazaki Hiroki; Anzai Naohiko; Endou Hitoshi
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo, Japan.
 SOURCE: Nephrology (Carlton, Vic.), (2011 Feb) Vol. 16, No. 2, pp. 156-62. Journal code: 9615568. E-ISSN: 1440-1797. L-ISSN: 1320-5358.
 PUB. COUNTRY: Australia
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 29 Jan 2011

Last Updated on STN: 29 Jan 2011

AB Aim: Hyperuricaemia is a significant factor in a variety of diseases, including gout and cardiovascular diseases. The kidney plays a dominant role in maintaining plasma urate levels through the excretion process. Human renal urate transporter URAT1 is thought to be an essential molecule that mediates the reabsorption of urate on the apical side of the proximal tubule. In this study the pharmacological characteristics and clinical implications of URAT1 were elucidated. Methods: Madin-Darby canine kidney (MDCK) cells stably expressing URAT1 (MDCK-URAT1) were established and examined the interactions of URAT1 with various drugs such as benzbromarone and its metabolites including 6-hydroxybenzbromarone, angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs and urate transport inhibitors including E3040 and probenecid. Results: MDCK-URAT1 cells exhibited a time- and dose-dependent increase in urate uptake, with a Km value of 570.7 $\mu\text{mol/L}$. When an URAT1-green fluorescent protein fusion protein construct was expressed in MDCK cells, the protein was sorted mainly to the apical side of the membrane. The drugs except for captopril dose-dependently inhibited urate uptake mediated by URAT1, with half maximal inhibitory concentration (IC(50)) values ranging 0.05-716 $\mu\text{mol/L}$. Conclusion: Comparing these IC(50) values with intratubular concentrations of unbound drugs in humans, it is thought that URAT1 is a target molecule of uricosuric drugs, including 6-hydroxybenzbromarone, probenecid, indomethacin and salicylate, to inhibit urate reabsorption in vivo. In addition, a cell line that stably expressing URAT1 could be a useful tool for the development of uricosuric drugs. .COPYRG. 2010 The Authors. Nephrology .COPYRG. 2010 Asian Pacific Society of Nephrology.

L3 ANSWER 23 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN DUPLICATE 9

ACCESSION NUMBER: 2007:380351 BIOSIS

DOCUMENT NUMBER: PREV200700380028

TITLE: Sodium-hydrogen exchanger regulatory factor-1 interacts with mouse urate transporter 1 to regulate renal proximal tubule uric acid transport.

AUTHOR(S): Cunningham, Rochelle [Reprint Author]; Brazie, Marc; Kanumuru, Srilatha; Xiaofei, E.; Biswas, Rajat; Wang, Fengying; Steplock, Deborah; Wade, James B.; Anzai, Naohiko; Endou, Hitoshi; Shenolikar, Shirish; Weinman, Edward J.

CORPORATE SOURCE: Univ Maryland, Sch Med, Dept Med, 22 S Greene St, Baltimore, MD 21201 USA

rcunning@medicine.umaryland.edu

SOURCE: Journal of the American Society of Nephrology, (MAY 2007) Vol. 18, No. 5, pp. 1419-1425. CODEN: JASNEU. ISSN: 1046-6673.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Jul 2007

Last Updated on STN: 4 Jul 2007

AB Sodium-hydrogen exchanger regulatory factor-1-deficient (NHERF-1(-/-)) mice demonstrate increases in the urinary excretion of phosphate, calcium, and uric acid associated with interstitial deposition of calcium in the papilla of the kidney. These studies examine the role of NHERF-1 in the tubular reabsorption of uric acid and regulation of mouse urate transporter 1 (mURAT1), a newly described transporter that is responsible for the renal tubular reabsorption of uric acid. In primary cultures of mouse renal proximal tubule cells, uric acid uptake was significantly lower in NHERF-1(-/-) cells compared with wild-type cells over a large

range of uric acid concentrations in the media. Western immunoblotting revealed a 56 +/- 6% decrease in the brush border membrane (BBM) expression of mURAT1 in NHERF-1(-/-) compared with wild-type control kidneys (P < 0.05). Confocal microscopy confirmed the reduced apical membrane expression of mURAT1 in NHERF-1(-/-) kidneys and demonstrated mislocalization of mURAT1 to intracellular vesicular structures. Para-aminohippurate significantly inhibited uric acid uptake in wild-type cells (41 +/- 2%) compared with NHERF-1(-/-) cells (8.2 +/- 3%). Infection of NHERF-1(-/-) cells with adenovirus-green fluorescence protein-NHERF-1 resulted in significantly higher rates of uric acid transport (15.4 +/- 1.1 pmol/mu g protein per 30 min) compared with null cells that were infected with control adenovirus- green fluorescence protein (7.9 +/- 0.3) and restoration of the inhibitory effect of para-aminohippurate (% inhibition 34 +/- 4%). These findings indicate that NHERF-1 exerts a significant effect on the renal tubular reabsorption of uric acid in the mouse by modulating the BBM abundance of mURAT1 and possibly other BBM uric acid transporters.

L3 ANSWER 24 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2010:381201 BIOSIS
DOCUMENT NUMBER: PREV201000381201
TITLE: Interaction of human renal urate transporters URAT1 with contrast media, lodipamide.
AUTHOR(S): Miura, Daisaku [Reprint Author]; Anzai, Naohiko; Khamdang, Suparat; Srivastava, Sunena; Amonpatumrat, Sirirat; Taejarernwiriyaikul, Ornjai; Kiyomiya, Ken-ichi; Sakurai, Hiroyuki; Endou, Hitoshi
CORPORATE SOURCE: Hyogo Univ Hlth Sci, Fac Pharm Sci, Dept Toxicol, Chuo Ku, Kobe, Hyogo 6508530, Japan
SOURCE: Journal of Pharmacological Sciences, (2010) Vol. 112, No. Suppl. 1, pp. 202P.
Meeting Info.: 83rd Annual Meeting of the Japanese-Pharmacological-Society. Osaka, JAPAN. March 16 -18, 2010. Japanese Pharmacol Soc.
ISSN: 1347-8613.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: Conference; (Meeting Poster)
ENTRY DATE: English
Entered STN: 1 Jul 2010
Last Updated on STN: 1 Jul 2010

L3 ANSWER 25 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2010:380679 BIOSIS
DOCUMENT NUMBER: PREV201000380679
TITLE: Elucidation of urate transport mechanism by analysis of renal urate transporters transgenic mice.
AUTHOR(S): Kimura, Toru [Reprint Author]; Tsukada, Ai; Amonpatumrat, Sirirat; Fukutomi, Toshiyuki; Jutabha, Promsuk; Ichida, Kimiyoshi; Kawahara, Katsumasa; Kanai, Yoshikatsu
CORPORATE SOURCE: Kyorin Univ, Sch Med, Dept Pharmacol Toxicol, Mitaka, Tokyo 1818611, Japan
SOURCE: Journal of Pharmacological Sciences, (2010) Vol. 112, No. Suppl. 1, pp. 66P.
Meeting Info.: 83rd Annual Meeting of the Japanese-Pharmacological-Society. Osaka, JAPAN. March 16 -18, 2010. Japanese Pharmacol Soc.
ISSN: 1347-8613.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jul 2010
Last Updated on STN: 1 Jul 2010

L3 ANSWER 26 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2010:147587 BIOSIS
DOCUMENT NUMBER: PREV201000147587
TITLE: GLUCOSE TRANSPORTER 9 (GLUT9) AS A SERUM URATE REGULATOR AND CAUSATIVE GENE FOR RENAL HYPOURICEMIA.
AUTHOR(S): Tadokoro, Shin [Reprint Author]; Matsuo, Hiroataka; Chiba, Toshinori; Nagamori, Shushi; Nakayama, Akiyoshi; Kitamura, Yousuke; Domoto, Hideharu; Phetdee, Kanokporn; Wiriyasermkul, Pattama; Nishiyama, Junichiro; Morimoto, Yuji; Kanai, Yoshikatsu; Shinomiya, Nariyoshi
CORPORATE SOURCE: Osaka Univ, Dept Pharmacol, Osaka, Japan
SOURCE: Journal of Physiological Sciences, (2009) Vol. 59, No. Suppl. 1, pp. 495.
Meeting Info.: 36th International Congress of Physiological Sciences (IUPS2009). Kyoto, JAPAN. July 27 -August 01, 2009. Int Union Physiol Sci.
ISSN: 1880-6546.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Mar 2010
Last Updated on STN: 10 Mar 2010

L3 ANSWER 27 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2009:292794 BIOSIS
DOCUMENT NUMBER: PREV200900293897
TITLE: Human urate transporter 1 (URAT1) mediates the transport of uric acid.
AUTHOR(S): Miura, Daisaku [Reprint Author]; Anzai, Naohiko; Tsukada, Ai; Kimura, Toru; Fukutomi, Toshiyuki; Kiyomiya, Ken-ichi; Sakurai, Hiroyuki; Endou, Hitoshi
CORPORATE SOURCE: Hyogo Univ Hlth Sci, Dept Pharm, Chuo Ku, Kobe, Hyogo 6508530, Japan
SOURCE: Journal of Pharmacological Sciences, (2009) Vol. 109, No. Suppl. 1, pp. 134P.
Meeting Info.: 82nd Annual Meeting of the Japanese-Pharmacological-Society. Yokohama, JAPAN. March 16 -18, 2009. Japanese Pharmacol Soc.
ISSN: 1347-8613.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 May 2009
Last Updated on STN: 6 May 2009

L3 ANSWER 28 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2010:144845 BIOSIS
DOCUMENT NUMBER: PREV201000144845
TITLE: TRANSPORTSOME IN RENAL ORGANIC SOLUTE TRANSPORT.
AUTHOR(S): Kanai, Yoshikatsu [Reprint Author]
CORPORATE SOURCE: Osaka Univ, Dept Pharmacol, Grad Sch Med, Suita, Osaka 565, Japan
SOURCE: Journal of Physiological Sciences, (2009) Vol. 59, No. Suppl. 1, pp. 35.
Meeting Info.: 36th International Congress of Physiological

Sciences (IUPS2009). Kyoto, JAPAN. July 27 -August 01,
2009. Int Union Physiol Sci.
ISSN: 1880-6546.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Mar 2010
Last Updated on STN: 10 Mar 2010

L3 ANSWER 29 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN

ACCESSION NUMBER: 2007:293536 BIOSIS
DOCUMENT NUMBER: PREV200700296988
TITLE: Human urate transporter URAT1 mediates the
transport of salicylate.
AUTHOR(S): Arizai, Naohiko [Reprint Author]; Nilwarangkoon, Sirinun;
Miura, Daisaku; Kofuji, Rie; Kanai, Yoshikatsu;
Endou, Hiroshi
CORPORATE SOURCE: Kyorin Univ, Sch Med, Dept Pharmacol Toxicol, Tokyo
1818611, Japan
SOURCE: Journal of Pharmacological Sciences, (2007) Vol. 103, No.
Suppl. 1, pp. 148P.
Meeting Info.: 80th Annual Meeting of the
Japanese-Pharmacological-Society. Nagoya, JAPAN. March 14
-16, 2007. Japanese Pharmacol Soc.
ISSN: 1347-8613.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 May 2007
Last Updated on STN: 9 May 2007

L3 ANSWER 30 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN

ACCESSION NUMBER: 2008:148283 BIOSIS
DOCUMENT NUMBER: PREV200800155779
TITLE: Renal urate transportsome: Toward the understanding of
pathogenetic role of renal urate handling for serum urate
disorders.
AUTHOR(S): Anzai, Naohiko [Reprint Author]; Kanai, Yoshikatsu
; Endou, Hitoshi
CORPORATE SOURCE: Kyorin Univ, Sch Med, Tokyo 1818611, Japan
SOURCE: Yakugaku Zasshi, (2007) Vol. 127, No. Suppl. 5, pp. 21-22.
Meeting Info.: 29th Symposium on Biomembrane-Drug
Interaction. Sendai, JAPAN. November 26 -27, 2007.
CODEN: YKKZAJ. ISSN: 0031-6903.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Feb 2008
Last Updated on STN: 10 Sep 2008

L3 ANSWER 31 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN

ACCESSION NUMBER: 2008:371790 BIOSIS
DOCUMENT NUMBER: PREV200800371789
TITLE: Effects of increased uric acid intake on the abundance of
URAT1 and organic anion transporter proteins in the
rat kidney.
AUTHOR(S): Kim, Gheun-Ho [Reprint Author]; Kim, Sua; Lee, Chang Hwa;
Kang, Chong Myung; Anzai, Naohiko; Endou, Hitoshi
CORPORATE SOURCE: Hanyang Univ, Coll Med, Dept Internal Med, Seoul 133791,

SOURCE: South Korea
Nephrology Dialysis Transplantation, (2007) Vol. 22, No.
Suppl. 6, pp. 18-19.
Meeting Info.: 44th ERA-EDTA Congress. Barcelona, SPAIN.
June 22 -24, 2007. ERA-EDTA.
ISSN: 0931-0509.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jul 2008
Last Updated on STN: 2 Jul 2008

L3 ANSWER 32 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2006:310047 BIOSIS
DOCUMENT NUMBER: PREV200600311107
TITLE: Recent advances in SLC22 organic anion transporters.
AUTHOR(S): Kanai, Yoshikatsu [Reprint Author]; Endou, Hitoshi
CORPORATE SOURCE: Kyorin Univ, Dept Pharmacol and Toxicol, Sch Med, Tokyo
1818611, Japan
SOURCE: Journal of Pharmacological Sciences, (2006) Vol. 100, No.
Suppl. 1, pp. 22P.
Meeting Info.: 79th Annual Meeting of the
Japanese-Pharmacological-Society. Yokohama, JAPAN. March 08
-10, 2006. Japanese Pharmacol Soc.
ISSN: 1347-8613.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2006
Last Updated on STN: 14 Jun 2006

L3 ANSWER 33 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2005:417531 BIOSIS
DOCUMENT NUMBER: PREV200510207362
TITLE: Regulation of renal urate transporter URAT1
transport function by PDZ domain protein PDZK1.
AUTHOR(S): Anzai, Naohiko [Reprint Author]; Miyazaki, Hiroki; Hirata,
Taku; He, Xin; Toki, Akie; Kanai, Yoshikatsu;
Endou, Hitoshi
CORPORATE SOURCE: Kyorin Univ, Sch Med, Dept Pharmacol Toxicol, Tokyo
1818611, Japan
SOURCE: Journal of Pharmacological Sciences, (2005) Vol. 97, No.
Suppl. 1, pp. 120P.
Meeting Info.: 78th Annual Meeting of the
Japanese-Pharmacological-Society. Yokohama, JAPAN. March 22
-24, 2005. Japanese Pharmacol Soc.
ISSN: 1347-8613.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Oct 2005
Last Updated on STN: 19 Oct 2005

L3 ANSWER 34 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2004:212443 BIOSIS
DOCUMENT NUMBER: PREV200400213996
TITLE: Gender and age difference of the expression of mouse urate
transporter (mURAT1).
AUTHOR(S): Hosoyamada, Makoto [Reprint Author]; Toki, Akie [Reprint

Author]; Nilwarangkoon, Sirinun [Reprint Author];
 Endou, Hitoshi [Reprint Author]
 CORPORATE SOURCE: Dept. Pharmacol. and Toxicol., Kyorin Univ. Sch. Med.,
 Shinkawa 6-20-2, Mitaka, Tokyo, Japan
 SOURCE: Journal of Pharmacological Sciences, (2004) Vol. 94, No.
 Supplement 1, pp. 260P. print.
 Meeting Info.: 77th Annual Meeting of the Japanese
 Pharmacological Society. Osaka, Japan. March 08-10, 2004.
 Japanese Pharmacological Society.
 ISSN: 1347-8613 (ISSN print).
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 14 Apr 2004
 Last Updated on STN: 14 Apr 2004

L3 ANSWER 35 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
 STN

ACCESSION NUMBER: 2005:89625 BIOSIS
 DOCUMENT NUMBER: PREV200500087089
 TITLE: Urate transporter: its regulation and clinical relevance.
 AUTHOR(S): Kanai, Yoshikatsu [Reprint Author]; Anzai,
 Naohiko; Hosoyamada, Makoto; Endou, Hitoshi
 CORPORATE SOURCE: Sch MedDept Pharmacol and Toxicol, Kyorin Univ, 6-20-2
 Shinkawa, Mitaka, Tokyo, 1818611, Japan
 SOURCE: Yakugaku Zasshi, (2004) Vol. 124, No. Suppl. 4, pp. 25-28.
 print.
 ISSN: 0031-6903 (ISSN print).
 DOCUMENT TYPE: Article
 LANGUAGE: Japanese
 ENTRY DATE: Entered STN: 2 Mar 2005
 Last Updated on STN: 2 Mar 2005

AB Urate, a naturally occurring product of purine metabolism, is present at
 higher levels in human blood than in other mammals, because humans have an
 effective renal urate reabsorption system, despite their evolutionary loss
 of hepatic uricase by mutational silencing. We identified the urate
 transporter in the human kidney (URAT1, encoded by SLC22A12), a
 urate anion exchanger regulating blood urate levels and targeted by
 uricosuric and antiuricosuric agents. We found that idiopathic renal
 hypouricaemia is due to the defects in SLC22A12. Because URAT1
 has a PDZ-binding motif at its C-terminus end, we performed yeast two
 hybrid screening to find out a multivalent PDZ domain-containing protein
 PDZK1 interacting with it. Coimmunoprecipitation studies revealed that
 the URAT1 directly interacts with PDZK1. The association of
 URAT1 with PDZK1 enhanced urate transport activities in HEK293
 cells, and the deletion of the URAT1 C-terminal PDZ motif
 abolished this effect. The augmentation of the transport activity was
 accompanied by a significant increase in the Vmax of urate transport via
 URAT1, and was associated with the increased surface expression
 level of URAT1 protein, indicating a novel role of PDZK1 in
 regulating the functional activity of URAT1-mediated urate
 transport in the apical membrane of renal proximal tubules.

L3 ANSWER 36 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
 STN

ACCESSION NUMBER: 2004:288189 BIOSIS
 DOCUMENT NUMBER: PREV200400286946
 TITLE: The multivalent PDZ domain protein PDZK1 upregulates the
 transport activity of renal urate-anion exchanger
 URAT1 via its C-terminal.
 AUTHOR(S): Anzai, Naohiko [Reprint Author]; Miyazaki, Hiroki; Hirata,
 Taku; Jutabha, Promsuk; Kanai, Yoshikatsu;

Endou, Hitoshi

CORPORATE SOURCE: Pharmacology and Toxicology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo, 181-8611, Japan
anzai@kyorin-u.ac.jp

SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 217.2.
http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB The urate/anion exchanger URAT1 regulates blood urate level and is expressed only in the kidney, where it is thought to participate in tubular urate reabsorption. We found that the multivalent PDZ domain-containing protein, PDZK1 interacts with URAT1 in a yeast two-hybrid screen. Such an interaction requires the PDZ motif of URAT1 in its extreme intracellular C-terminal region as identified by both yeast two-hybrid and in vitro binding assays. In addition, the first, second, and fourth PDZ domains within PDZK1 associate with the URAT1 C-terminal. Co-immunoprecipitation studies revealed that the wild-type URAT1, but not its mutant lacking the PDZ-motif, directly interacts with PDZK1. When transfected into HEK293 cells with pDsRed2-C1/PDZK1 and pEGFP-C2/ wild-type URAT1, PDZK1 colocalized with URAT1 on the surface membrane. The association of URAT1 with PDZK1 enhanced urate transport activities in HEK293 cells (1.4-folds), and the deletion of the URAT1 C-terminal PDZ motif abolished this effect. The augmentation of the transport activity was accompanied by a significant increase in the Vmax of urate transport via URAT1, although it was not associated with the high URAT1 protein level in crude membrane fractions from URAT1-expressing HEK293 cells prepared with or without PDZK1 transfection. Taken together, the present study indicates the novel role of PDZK1 in regulating the functional activity of URAT1-mediated urate transport in the membrane of renal proximal tubules.

L3 ANSWER 37 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:92175 BIOSIS

DOCUMENT NUMBER: PREV200400085367

TITLE: Interaction of the PDZ domain protein PDZK1 with urate/anion exchanger URAT1.

AUTHOR(S): Miyazaki, Hiroki [Reprint Author]; Anzai, Naohiko [Reprint Author]; Hirata, Taku [Reprint Author]; Iribe, Yuji [Reprint Author]; Nonoguchi, Hiroshi; Kanai, Yoshikatsu [Reprint Author]; Tomita, Kimio; Endou, Hitoshi [Reprint Author]

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Mitaka City, Tokyo, Japan

SOURCE: Journal of the American Society of Nephrology, (November 2003) Vol. 14, No. Abstracts Issue, pp. 307A. print.
Meeting Info.: Meeting of the American Society of Nephrology Renal Week. San Diego, CA, USA. November 12-17, 2003. American Society of Nephrology.
CODEN: JASNEU. ISSN: 1046-6673.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Feb 2004
Last Updated on STN: 11 Feb 2004

L3 ANSWER 38 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2004:93227 BIOSIS
DOCUMENT NUMBER: PREV200400086419
TITLE: Expression of a urate transporter in human vascular smooth
muscle cells.
AUTHOR(S): Price, Karen L. [Reprint Author]; Mu, Wei [Reprint Author];
Raines, Elaine W.; Long, David A.; Endou, Hitoshi
; Johnson, Richard J. [Reprint Author]
CORPORATE SOURCE: Nephrology Unit, Baylor College of Medicine, Houston, TX,
USA
SOURCE: Journal of the American Society of Nephrology, (November
2003) Vol. 14, No. Abstracts Issue, pp. 145A. print.
Meeting Info.: Meeting of the American Society of
Nephrology Renal Week. San Diego, CA, USA. November 12-17,
2003. American Society of Nephrology.
CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 2004
Last Updated on STN: 11 Feb 2004

L3 ANSWER 39 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2003:204555 BIOSIS
DOCUMENT NUMBER: PREV200300204555
TITLE: Transport function and renal localization of mouse
homologue of urate transporter URAT1.
AUTHOR(S): Hosoyamada, Makoto [Reprint Author]; Toki, Akie [Reprint
Author]; Urano, Wako [Reprint Author]; Endou,
Hitoshi [Reprint Author]
CORPORATE SOURCE: Dept. Pharmacol. Toxicol., Sch. Med., Kyorin Univ., Mitaka,
181-8611, Japan
SOURCE: Journal of Pharmacological Sciences, (2003) Vol. 91, No.
Supplement I, pp. 72P. print.
Meeting Info.: 76th Annual Meeting of the Japanese
Pharmacological Society. Fukuoka, Japan. March 24-26, 2003.
Japanese Pharmacological Society.
ISSN: 1347-8613 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Apr 2003
Last Updated on STN: 23 Apr 2003

L3 ANSWER 40 OF 53 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2002:567174 BIOSIS
DOCUMENT NUMBER: PREV200200567174
TITLE: Mutations in URAT1 gene in the familial renal
hypouricemia.
AUTHOR(S): Kitamura, Kenichiro [Reprint author]; Wakita, Naoki
[Reprint author]; Adachi, Masataka [Reprint author]; Tuyen,
Do-Gia [Reprint author]; Nonoguchi, Hiroshi [Reprint
author]; Hosoyamada, Makoto; Endou, Hitoshi;
Tomita, Kimio [Reprint author]
CORPORATE SOURCE: Third Department of Internal Medicine, Kumamoto University
School of Medicine, Kumamoto, Japan

SOURCE: Journal of the American Society of Nephrology, (September, 2002) Vol. 13, No. Program and Abstracts Issue, pp. 64A.
print.
Meeting Info.: Meeting of the American Society of Nephrology. Philadelphia, PA, USA. October 30-November 04, 2002. American Society of Nephrology.
CODEN: JASNEU. ISSN: 1046-6673.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

L3 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2010:1240276 CAPLUS

TITLE: Renal solute transporters and their relevance to serum urate disorder

AUTHOR(S): Anzai, Naohiko; Jutabha, Promsuk; Endou, Hitoshi

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Mitaka-shi, Tokyo, 181-8611, Japan

SOURCE: Current Hypertension Reviews (2010), 6(3), 148-154
CODEN: CHRUDH; ISSN: 1573-4021
URL: http://www.benthamdirect.org/pages/b_viewarticle.php

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB Since uric acid (urate), the final product of purine metabolism, exhibits antioxidative activity, its protective role against oxidative stress becomes attractive. Low serum urate levels have been associated with multiple sclerosis, Parkinson's disease, and Alzheimer's disease. Despite its beneficial role, hyperuricemia is associated with gout, hypertension, cardiovascular diseases such as myocardial infarction and stroke, and renal diseases such as acute urate nephropathy and nephrolithiasis. The urate transport system of the kidney is an important determinant of the serum urate level, but clarification of its mol. mechanism remains incomplete. In 2002, our group identified URAT1 (SLC22A12), a renal apical urate/anion exchanger, leading to the accumulation of information concerning individual mols. involved in urate transport in the kidney. In 2008, we functionally characterized facilitatory glucose transporter family member GLUT9 (SLC2A9) as a voltage-driven urate transporter URATv1 and anal. of a renal hypouricemia patient with a genetic defect in SLC2A9 have established the main route of the urate reabsorption pathway at the basolateral side of renal proximal tubules, where urate in the urinary lumen is taken up via apical URAT1 and intracellular urate exits from the cell to the interstitium/blood space via basolateral URATv1. In this review, recent findings concerning these mols. are presented.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2007:1179955 CAPLUS

DOCUMENT NUMBER: 148:68744

TITLE: Drug discovery for hyperuricemia

AUTHOR(S): Anzai, Naohiko; Endou, Hitoshi

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Kyorin University School of Medicine, 6-20-2, Shinkawa,

SOURCE: Mitaka-shi, Tokyo, 181-8611, Japan
Expert Opinion on Drug Discovery (2007), 2(9),
1251-1261
CODEN: EODDBX; ISSN: 1746-0441

PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Hyperuricemia is associated with an increased risk of developing gout. This increases with the degree and duration of hyperuricemia. Gout can be managed by dietary modification and pharmacol. urate-lowering therapies. The recent identification of the renal apical urate/anion exchanger URAT1 (SLC22A12) and several membrane proteins relevant to the transport of urate play an important role in gaining a better understanding of the mode of action of many drugs used to treat gout. As described in this review, therapeutics designed to modify URAT1 transport activities might be useful in treating pathologies associated with hyperuricemia such as gout and urolithiasis. Continuing studies into the urate transportsome hold promise for the development of new, more effective therapeutics for hyperuricemia.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:451230 CAPLUS
DOCUMENT NUMBER: 142:457093

TITLE: Remedy/preventive for vascular disorders and hypertension and method of screening the same

INVENTOR(S): Endou, Hitoshi; Kanai, Yoshikatsu; Johnson, Richard J.; Price, Karen Leigh

PATENT ASSIGNEE(S): Human Cell Systems, Inc., Japan

SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046724	A1	20050526	WO 2004-JP16761	20041111
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1698348	A1	20060906	EP 2004-799622	20041111
R: DE, FR, GB				
US 20090312415	A1	20091217	US 2008-579173	20081204
PRIORITY APPLN. INFO.:			JP 2003-384863	A 20031114
			WO 2004-JP16761	W 20041111

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB It is intended to clarify a transportation system participating in the uric acid uptake in vascular smooth muscle cells (VSMCs) and provide a novel remedy, a preventive or a treating agent for vascular disorders,

hypertension and renal disorders with the use of a drug participating in this transportation system. It is also intended to provide a novel screening system for a remedy, a preventive or a treating agent for vascular disorders, hypertension and renal disorders with the use of such a transportation system. Namely, a medicinal composition for healing, preventing or treating vascular disorders, hypertension and renal disorders which comprises a drug having an effect of inhibiting the uric acid uptake by a uric acid transporter URAT1 and a pharmaceutically acceptable carrier; and a method of screening a substance efficacious for healing, preventing or treating vascular disorders, hypertension and renal disorders which comprises using a cell line expressing URAT1 in the presence or absence of a test compound and assaying the uric acid uptake level, cell proliferation ability or the amount of a monocyte chemotactic factor produced by the cells.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:975264 CAPLUS

DOCUMENT NUMBER: 144:86020

TITLE: A common mutation in an organic anion transporter gene, SLC22A12, is a suppressing factor for the development of gout

AUTHOR(S): Taniguchi, Atsuo; Urano, Wako; Yamanaka, Mariko; Yamanaka, Hisashi; Hosoyamada, Makoto; Endou, Hitoshi; Kamatani, Naoyuki

CORPORATE SOURCE: Japan

SOURCE: Arthritis & Rheumatism

(2005), 52(8), 2576-2577

CODEN: ARHEAW; ISSN: 0004-3591

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this study, SLC22A12 in patients with gout was examined to analyze the roles of SLC22A12 in the development of gout. A total of 185 male Japanese patients with primary gout who attended the outpatient clinic at the Institute of Rheumatol., Tokyo Women's Medical University, were randomly selected for the study. This study showed that the G774A mutation in SLC22A12 not only lowers serum uric acid levels in both men and women, but also prevents the development of gout in men. Since all study subjects were Japanese, the role of this mutation in other ethnic groups remains to be determined. In addition, all of the gout patients in this study were men. The role of the G774A mutation in women with gout should be clarified in another study. The relationship between the G774A mutation and hypouricemia has previously been reported, and the findings of the present study extend the clin. significance of URAT1 to gout. There are germline mutations that promote the development of gout as well as germline mutations that prevent it.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:351077 CAPLUS

DOCUMENT NUMBER: 142:371924

TITLE: Mutations in human urate transporter 1 gene in presecretory reabsorption defect type of familial renal hypouricemia

AUTHOR(S): Wakida, Naoki; Tuyen, Do Gia; Adachi, Masataka; Miyoshi, Taku; Nonoguchi, Hiroshi; Oka, Toshiaki; Ueda, Osamu; Tazawa, Masahiro; Kurihara, Satoshi;

Yoneta, Yoshitaka; Shimada, Hajime; Oda, Takashi;
Kikuchi, Yuichi; Matsuo, Hirota; Hosoyamada, Makoto;
Endou, Hitoshi; Otagiri, Masaki; Tomita,
Kimio; Kitamura, Kenichiro

CORPORATE SOURCE: Department of Nephrology, Kumamoto University Graduate
School of Medical and Pharmaceutical Sciences,
Kumamoto, 860-8556, Japan

SOURCE: Journal of Clinical Endocrinology and Metabolism
(2005), 90(4), 2169-2174
CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To date, 11 loss of function mutations in the human urate transporter 1 (hURAT1) gene have been identified in subjects with idiopathic renal hypouricemia. In the present studies the authors investigated the clinical features and the mutations in the hURAT1 gene in seven families with presecretory resorption defect-type renal hypouricemia and in one family with the postsecretory resorption defect type. Twelve affected subjects and 26 family members were investigated. Mutations were analyzed by PCR and the direct sequencing method. Urate-transporting activities of wild-type and mutant hURAT1 were determined by [¹⁴C]urate uptake in *Xenopus* oocytes. Mutational analysis revealed three previously reported mutations (G774A, A1145T, and 1639-1643 del-GTCCCT) and a novel mutation (T1253G) in families with the presecretory resorption defect type. Neither mutations in the coding region of hURAT1 gene nor significant segregation patterns of the hURAT1 locus were detected in the postsecretory resorption defect type. All hURAT1 mutants had significantly reduced urate-transporting activities compared with wild type, suggesting that T1253G is a loss of function mutation, and hURAT1 is responsible for the presecretory resorption defect-type familial renal hypouricemia. Future studies are needed to identify a responsible gene for the postsecretory resorption defect-type familial renal hypouricemia.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS
RECORD (15 CITINGS)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:1255892 CAPLUS

DOCUMENT NUMBER: 145:43266

TITLE: Urate transporter 1 (URAT1)

AUTHOR(S): Kanai, Yoshikatsu

CORPORATE SOURCE: School of Medicine, Dep. of Pharmacology, Kyorin
University, 6-20-2 Shinkawa, Mitaka-shi, Tokyo,
181-8611, Japan

SOURCE: Jin to Toseki (2005), 59(4), 586-588

CODEN: JTIOAA; ISSN: 0385-2156

PUBLISHER: Tokyo Igakusha

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review, on the structure and function of URAT1 and roles of
URAT1 gene mutation in pathogenesis of diseases.

L3 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:1085903 CAPLUS

DOCUMENT NUMBER: 144:188720

TITLE: Uric Acid Causes Vascular Smooth Muscle Cell

Proliferation by Entering Cells via a Functional Urate
Transporter

AUTHOR(S): Kang, Duk-Hee; Han, Lin; Ouyang, Xiaosen; Kahn, Andrew
M.; Kanellis, John; Li, Ping; Feng, Lili; Nakagawa,

Takahiko; Watanabe, Susumu; Hosoyamada, Makoto; Endou, Hitoshi; Lipkowitz, Michael; Abramson, Ruth; Mu, Wei; Johnson, Richard J.

CORPORATE SOURCE: Division of Nephrology, Ewha Women's University College of Medicine, Seoul, S. Korea

SOURCE: American Journal of Nephrology (2005), 25(5), 425-433
CODEN: AJNED9; ISSN: 0250-8095

PUBLISHER: Karger

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Soluble uric acid stimulates vascular smooth muscle cell (VSMC) proliferation by activating mitogen-activated protein kinases, and stimulating COX-2 and PDGF synthesis. The mechanism by which uric acid enters the VSMC is not known. We hypothesized that uric acid enters via transporters similar to that observed in the kidney. Methods: We studied the uptake of uric acid into rat VSMC under polarized and depolarized conditions and in the presence of organic anion transport (OAT) inhibitors (probenecid and benzbromarone) or p-aminohippurate (PAH). We also examined the ability of probenecid to inhibit uric acid-induced VSMC proliferation and monocyte chemoattractant protein-1 (MCP-1) synthesis. Results: 14C-Urate uptake was shown in VSMC and was enhanced under depolarized conditions. 14C-Uric acid uptake was inhibited by probenecid and benzbromarone, as well as by unlabeled urate and PAH. Probenecid blocked VSMC proliferation and MCP-1 expression in response to uric acid. VSMC did not express rOAT1-3, rOAT-5 or URAT-1 mRNA by PCR, but did express the voltage-sensitive transporter (UAT) by both PCR and RNase protection assay. Conclusions: Urate enters VSMC by both voltage-sensitive and OAT pathways, and the uptake, cell proliferation and MCP-1 expression can be blocked by OAT inhibitors. The specific transporter(s) responsible for the urate uptake remains to be determined

OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:260385 CAPLUS

DOCUMENT NUMBER: 143:130616

TITLE: Transport dysfunction of renal proximal tubules from physiological aspects

AUTHOR(S): Kanai, Yoshikatsu

CORPORATE SOURCE: School of Medicine, Dept. of Pharmacology, Kyorin University, Mitaka, Tokyo, 181-8611, Japan

SOURCE: Jin to Toseki (2005), 58(2), 185-189
CODEN: JTIOAA; ISSN: 0385-2156

PUBLISHER: Tokyo Igakusha

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review. The topics discussed are (1) amino acid transporter SLC6A19 gene mutation in Hartnup disorder; (2) urate transporter 1 (URAT1) deficiency in hereditary renal hypouricemia; and (3) URAT1 binding protein PDZK1 and PDZK1 in the regulation of URAT1.

L3 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:338833 CAPLUS

DOCUMENT NUMBER: 142:389838

TITLE: Disorders of membrane transporters and diseases: an overview

AUTHOR(S): Anzai, Naohiko; Hirota, Taku; Endou, Hitoshi

CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Kyorin Univ. Sch. Med., Japan

SOURCE: Rinsho Kagaku (Nippon Rinsho Kagakkai) (2005), 34(1),

PUBLISHER: Nippon Rinsho Kagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on diseases caused by transporter disorders, discussing diseases associated with genetic mutations in organic ion transporters including urate transporter URAT1 and carnitine transporters, association of cation transporter OCTN1 mutation and autoimmune diseases, diseases involved in amino acid transporters, and monocarbonate transporter MCT8 mutations and X-linked mental retardation.

L3 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2004:229718 CAPLUS

DOCUMENT NUMBER: 140:282796

TITLE: Molecular biology of urate transporter

AUTHOR(S): Anzai, Naohiko; Miyazaki, Hiroki; Endou, Hitoshi

CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Kyoto Univ. Sch. Med., Mitaka, 181-8611, Japan

SOURCE: Seikagaku (2004), 76(2), 101-110

CODEN: SEIKAQ; ISSN: 0037-1017

PUBLISHER: Nippon Seikagakkai

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review on physiol. significance of urate, 4-component model of urate transport in the kidney, urate transport in the proximal tubule, cloning of organic ion transporter (SLC22), cloning of a novel kidney-specific urate transporter (URAT1) involved in urate resorption, other urate transporters (UAT/galectin 9 and OATv1), role of PDZ protein in functional regulation of urate transporters, and intracellular binding protein (PDZK1) of URAT1.

L3 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2004:870865 CAPLUS

DOCUMENT NUMBER: 142:50813

TITLE: The urate transporters

AUTHOR(S): Hosoyama, Makoto; Kanai, Yoshikatsu; Endou, Hitoshi

CORPORATE SOURCE: School of Medicine, Dep. of Pharmacology, Kyorin University, Japan

SOURCE: Tsufu to Kakusan Taisha (2004), 28(1), 1-5

CODEN: TKTAF7; ISSN: 1344-9796

PUBLISHER: Nippon Tsufu Kakusan Taisha Gakkai

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review, on urate transporters (URAT1, OAT1, OAT3, OAT4, and UAT/LGLS), with resp. to their mol. structures, tissue expression, and functions.

L3 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2003:712638 CAPLUS

DOCUMENT NUMBER: 140:125983

TITLE: Urate transporter and idiopathic renal hypouricemia

AUTHOR(S): Yokoyama, Hirokazu; Anzai, Naohiko; Endou, Hitoshi

CORPORATE SOURCE: School of Medicine, Dep. of Pharmacology, Kyorin University, Japan

SOURCE: Molecular Medicine (Tokyo, Japan) (2003), 40(7), 762-767

CODEN: MOLMEL; ISSN: 0918-6557

PUBLISHER: Nakayama Shoten

DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. The topics discussed are (1) biol. significance of uric acid;
(2) uric acid transport in kidney; (3) urate transporter 1 (URAT1
); (4) uric acid transport at renal proximal tubule cells; (5) drugs
affecting URAT1; (6) mutations of URAT1 causing
idiopathic renal hypouricemia; and (7) regulation of uric acid transporter
URAT1 through interaction with intracellular proteins.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

L3 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2003:360223 CAPLUS
DOCUMENT NUMBER: 138:382849
TITLE: Transporters and disease
AUTHOR(S): Endou, Hitoshi; Yokoyama, Hirokazu
CORPORATE SOURCE: Sch. Med., Kyorin Univ., Japan
SOURCE: Farumashia (2003), 39(5), 431-435
CODEN: FARUAW; ISSN: 0014-8601
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on diseases caused by genetic alterations of drug transporters,
focusing on uric acid transporter URAT1, carnitine transporter
OCTN2/CT1, ABC transporters, and amino acid transporters.

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=> S (MCP-1 OR (monocyte chemotactic factor)) (P) (uric OR urate OR URAT1) AND
 pd<=20041111
 L1 32 (MCP-1 OR (MONOCYTE CHEMOTACTIC FACTOR)) (P) (URIC OR URATE OR
 URAT1) AND PD<=20041111

=> Dup Rem L1
PROCESSING COMPLETED FOR L1
L2 12 DUP REM L1 (20 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE MEDLINE
ANSWERS '10-11' FROM FILE BIOSIS
ANSWER '12' FROM FILE CAPLUS

=> D ibib abs L2 1-12

L2 ANSWER 1 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004629737 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15471869
TITLE: Signaling events involved in macrophage chemokine
expression in response to monosodium urate crystals.
AUTHOR: Jaramillo Maritza; Godbout Marianne; Naccache Paul H;
Olivier Martin
CORPORATE SOURCE: Research Institute of the McGill University Health Centre,
Centre for the Study of Host Resistance, Department of
Medicine, McGill University, Montreal, Quebec H3A 2B4,
Canada.
SOURCE: The Journal of biological chemistry, (2004 Dec 10)
Vol. 279, No. 50, pp. 52797-805. Electronic Publication:
2004-10-07.
Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 21 Dec 2004
Last Updated on STN: 2 Feb 2005
Entered Medline: 1 Feb 2005
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB Chemokine production has been associated with leukocyte infiltration into
the joint during gouty arthritis, and monosodium urate (MSU)
crystals, the causative agent of this arthropathy, have been shown to
modulate their expression. In the present study, we investigated the
transductional mechanisms underlying this cellular regulation in the
murine macrophage cell line B10R. We report that MSU crystals rapidly and
transiently increase mRNA levels of various chemokines in a
concentration-dependent manner. Examination of second messenger
activation revealed that macrophage exposure to MSU crystals led to
MEK1/2, ERK1/2, and inhibitory protein kappaBalpha phosphorylation as well
as to NF-kappaB and AP-1 nuclear translocation. Of interest, specific
blockage of the ERK1/2 pathway drastically reduced up-modulation of MSU
crystal-mediated chemokine production and activation of nuclear factors.
Similarly, selective inhibition of NF-kappaB suppressed NF-kappaB DNA
binding activity and the induction of all chemokine transcripts. These
findings indicate that ERK1/2-dependent signals seem to be required for
AP-1 and NF-kappaB activation and subsequent mRNA expression of the
various macrophage chemokines. In addition, transcription and stability
assays performed in presence of actinomycin D showed that MSU
crystal-mediated MIP-1beta mRNA up-regulation resulted solely from
transcriptional control, whereas that of MIP-1alpha, MIP-2, and
MCP-1 was due to both gene transcription activation and
mRNA posttranscriptional stabilization. Overall, the results of this
study help to define the molecular events that govern macrophage chemokine
regulation in response to MSU crystals, which is of paramount importance
to better understand, and eventually to tame, the inflammatory response
during acute gout.

L2 ANSWER 2 OF 12 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2004541378 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15514269
 TITLE: Consumption of high-pressure vegetable soup increases plasma vitamin C and decreases oxidative stress and inflammatory biomarkers in healthy humans.
 AUTHOR: Sanchez-Moreno Concepcion; Cano M Pilar; de Ancos Begona; Plaza Lucia; Olmedilla Begona; Granado Fernando; Martin Antonio
 CORPORATE SOURCE: Nutrition and Neurocognition Laboratory, Jean Mayer U.S.D.A. Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA.
 SOURCE: The Journal of nutrition, (2004 Nov) Vol. 134, No. 11, pp. 3021-5.
 Journal code: 0404243. ISSN: 0022-3166. L-ISSN: 0022-3166.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200412
 ENTRY DATE: Entered STN: 30 Oct 2004
 Last Updated on STN: 20 Dec 2004
 Entered Medline: 9 Dec 2004

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
 AB Current evidence supports a significant association between fruit and vegetable intake and health. In this study, we assessed the effect of consuming a vegetable-soup "gazpacho" on vitamin C and biomarkers of oxidative stress and inflammation in a healthy human population. We also examined the association between vitamin C and F(2)-isoprostanes (8-epiPGF(2alpha)), uric acid (UA), prostaglandin E(2) (PGE(2)), monocyte chemoattractant protein-1 (MCP-1), and the cytokines, tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and IL-6. Gazpacho is a Mediterranean dish defined as a ready-to-use vegetable soup, containing approximately 80% crude vegetables rich in vitamin C. Subjects (6 men, 6 women) enrolled in this study consumed 500 mL/d of gazpacho corresponding to an intake of 72 mg of vitamin C. On d 1, subjects consumed the gazpacho in one dose; from d 2 until the end of the study, d 14, 250 mL was consumed in the morning and 250 mL in the afternoon. Blood was collected before drinking the soup (baseline) and on d 7 and 14. Baseline plasma vitamin C concentrations did not differ between men and women (P = 0.060). Compared with baseline, the vitamin C concentration was significantly higher on d 7 and 14 of the intervention in both men and women (P < 0.05). Baseline plasma levels of UA and F(2)-isoprostanes were higher (P < or = 0.002) in men than in women. The F(2)-isoprostanes decreased on d 14 in men and women (P < or = 0.041), and UA decreased in men (P = 0.028). The concentrations of vitamin C and 8-epiPGF(2alpha) were inversely correlated (r = -0.585, P = 0.0002). Plasma PGE(2) and MCP-1 concentrations decreased in men and women (P < or = 0.05) on d 14, but those of TNF-alpha, IL-1beta, and IL-6 did not change. Consumption of the vegetable soup decreases oxidative stress and biomarkers of inflammation, which indicates that the protective effect of vegetables may extend beyond their antioxidant capacity.

L2 ANSWER 3 OF 12 MEDLINE on STN DUPLICATE 3
 ACCESSION NUMBER: 2004000422 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14671251
 TITLE: Decreased levels of plasma vitamin C and increased concentrations of inflammatory and oxidative stress markers

after stroke.

AUTHOR: Sanchez-Moreno Concepcion; Dashe John F; Scott Tammy; Thaler David; Folstein Marshal F; Martin Antonio

CORPORATE SOURCE: Nutrition and Neurocognition Laboratory, Jean Mayer USDA-Human Nutrition Research Center on Aging, Boston, Mass 02111, USA.

SOURCE: Stroke; a journal of cerebral circulation, (2004 Jan) Vol. 35, No. 1, pp. 163-8. Electronic Publication: 2003-12-11. Journal code: 0235266. E-ISSN: 1524-4628. L-ISSN: 0039-2499.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200401

ENTRY DATE: Entered STN: 2 Jan 2004
Last Updated on STN: 27 Jan 2004
Entered Medline: 26 Jan 2004

OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record

AB BACKGROUND AND PURPOSE: Inflammatory response is a critical component of the complex pathophysiological response to stroke. Vitamin C has been shown to have important roles in cell performance and vascular function. In this study, we compared the nutritional status and levels of inflammatory markers between stroke cases and controls and assessed which antioxidant was associated with levels of inflammatory markers and oxidative stress among cases and controls.

METHODS: We evaluated the nutritional status and measured plasma levels of vitamins C and E, uric acid, serum levels of C-reactive protein (CRP), the cytokines tumor necrosis factor-alpha and interleukin-1beta, intercellular adhesion molecule-1 (ICAM-1) and chemokine monocyte chemoattractant protein-1 (MCP-1), prostaglandins PGE2 and PGI2, and 8-isoprostanes (8-epiPGF2alpha) for 15 patients with ischemic stroke within 2 to 5 days after stroke onset and for 24 control subjects.

RESULTS: Stroke patients had significantly lower plasma levels of vitamin C than did controls. Among stroke patients, CRP was significantly elevated, as were the ICAM-1, MCP-1, and 8-epiPGF2alpha, but the prostaglandins PGE2 and PGI2 were significantly reduced. Interestingly, vitamin C concentration was significantly inversely correlated with the levels of CRP and 8-epiPGF2alpha among stroke patients, and 8-epiPGF2alpha was significantly associated with the levels of CRP. Uric acid was also elevated among stroke patients.

CONCLUSIONS: Lower vitamin C concentration, higher serum levels of inflammatory (CRP, ICAM-1, MCP-1) and oxidative stress (8-epiPGF2alpha) markers, and lower PGI2 and PGE2 concentrations among stroke patients indicate the presence of an inflammatory response associated with stroke.

L2 ANSWER 4 OF 12 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2004332384 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15235923

TITLE: Crystal-induced inflammation of the kidneys: results from human studies, animal models, and tissue-culture studies.

AUTHOR: Khan Saeed R

CORPORATE SOURCE: Department of Pathology, College of Medicine, University of

Florida, Gainesville, FL 32610-0275, USA.
 khan@pathology.ufl.edu
 DK-59765 (United States NIDDK NIH HHS)
 R01 DK-53962 (United States NIDDK NIH HHS)
 SOURCE: Clinical and experimental nephrology, (2004 Jun)
 Vol. 8, No. 2, pp. 75-88. Ref: 150
 Journal code: 9709923. ISSN: 1342-1751. L-ISSN: 1342-1751.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200412
 ENTRY DATE: Entered STN: 7 Jul 2004
 Last Updated on STN: 23 Dec 2004
 Entered Medline: 22 Dec 2004

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
 REFERENCE COUNT: 150 There are 150 cited references for this document.

AB Calcium oxalate (CaOx), calcium phosphate (CaP), and uric acid
 or urate are the most common crystals seen in the kidneys. Most
 of the crystals evoke an inflammatory response leading to fibrosis, loss
 of nephrons, and eventually to chronic renal failure. Of the three, CaOx
 monohydrate is the most reactive, whereas some forms of CaP do not evoke
 any discernible response. Reactive oxygen species are produced during the
 interactions between the crystals and renal cells and are responsible for
 the various cellular responses. CaOx crystals generally form in the renal
 tubules. Exposure of renal epithelial cells to CaOx crystals results in
 the increased synthesis of osteopontin, bikunin, heparan sulfate, monocyte
 chemoattractant protein 1 (MCP-1), and prostaglandin
 (PG) E2, which are known to participate in inflammatory processes and in
 extracellular matrix production. CaOx crystal deposition in rat kidneys
 also activates the renin-angiotensin system. Both Ox and CaOx crystals
 selectively activate p38 mitogen-activated protein kinase (MAPK) in
 exposed tubular cells. CaP crystals can form in the tubular lumen,
 tubular cells, or tubular basement membrane. Renal epithelial cells
 exposed to brushite crystals produce MCP-1. Basic CaP
 and calcium pyrophosphate dihydrate induce mitogenesis in fibroblasts,
 stimulate production of PGE2, and up-regulate the synthesis of
 metalloproteinases (MMP) while down-regulating the production of
 inhibitors of MMPs through activation of p42/44 MAPK. Deposition of
 urate crystals in the kidneys becomes associated with renal
 tubular atrophy, interstitial fibrosis, and development of inflammatory
 infiltrate. Renal epithelial cells exposed to uric acid
 crystals synthesize MCP-1 as well as PGE2. Monocytes
 or neutrophils exposed to urate crystals produce tumor necrosis
 factor alpha, interleukin-1 (IL-1), IL-6, and IL-8. Expression of IL-8 is
 mediated through extracellular signal-regulated kinase 1 (ERK-1)/ERK-2 and
 nuclear transcription factors activated protein 1 and nuclear factor
 kappa-beta. Urate crystals also stimulate the macrophages to
 produce MMPs.

L2 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 5
 ACCESSION NUMBER: 2003265380 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12743010
 TITLE: Uric acid stimulates monocyte chemoattractant protein-1
 production in vascular smooth muscle cells via
 mitogen-activated protein kinase and cyclooxygenase-2.
 AUTHOR: Kanellis John; Watanabe Susumu; Li Jin H; Kang Duk Hee; Li
 Ping; Nakagawa Takahiko; Wamsley Ann; Sheikh-Hamad David;
 Lan Hui Y; Feng Lili; Johnson Richard J
 CORPORATE SOURCE: Division of Nephrology, Baylor College of Medicine,

SM-1273, 6550 Fannin St, Houston TX 77030.
rjohnson@bcm.tmc.edu
CONTRACT NUMBER: 1P50DK-064233-01 (United States NIDDK NIH HHS)
HL 68607 (United States NHLBI NIH HHS)
SOURCE: Hypertension, (2003 Jun) Vol. 41, No. 6, pp.
1287-93. Electronic Publication: 2003-05-12.
Journal code: 7906255. E-ISSN: 1524-4563. L-ISSN:
0194-911X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 8 Jun 2003
Last Updated on STN: 28 Jun 2003
Entered Medline: 27 Jun 2003
OS.CITING REF COUNT: 25 There are 25 MEDLINE records that cite this record
AB Previous studies have reported that uric acid stimulates
vascular smooth muscle cell (VSMC) proliferation in vitro. We
hypothesized that uric acid may also have direct proinflammatory
effects on VSMCs. Crystal- and endotoxin-free uric acid was
found to increase VSMC monocyte chemoattractant protein-1 (MCP-
1) expression in a time- and dose-dependent manner, peaking at 24
hours. Increased mRNA and protein expression occurred as early as 3 hours
after uric acid incubation and was partially dependent on
posttranscriptional modification of MCP-1 mRNA. In
addition, uric acid activated the transcription factors nuclear
factor-kappaB and activator protein-1, as well as the MAPK signaling
molecules ERK p44/42 and p38, and increased cyclooxygenase-2 (COX-2) mRNA
expression. Inhibition of p38 (with SB 203580), ERK 44/42 (with U0126 or
PD 98059), or COX-2 (with NS398) each significantly suppressed
uric acid-induced MCP-1 expression at 24
hours, implicating these pathways in the response to uric acid.
The ability of both n-acetyl-cysteine and diphenyleneonium (antioxidants)
to inhibit uric acid-induced MCP-1
production suggested involvement of intracellular redox pathways.
Uric acid regulates critical proinflammatory pathways in VSMCs,
suggesting it may have a role in the vascular changes associated with
hypertension and vascular disease.

L2 ANSWER 6 OF 12 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003123481 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12637633
TITLE: Increased expression of monocyte chemoattractant protein-1
(MCP-1) by renal epithelial cells in
culture on exposure to calcium oxalate, phosphate and
uric acid crystals.
AUTHOR: Umekawa Tohru; Chegini Nasser; Khan Saeed R
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University
of Florida College of Medicine, Gainesville, FL 32610-0275,
USA.
CONTRACT NUMBER: DK59765 (United States NIDDK NIH HHS)
R01 DK53962 (United States NIDDK NIH HHS)
SOURCE: Nephrology, dialysis, transplantation : official
publication of the European Dialysis and Transplant
Association - European Renal Association, (2003
Apr) Vol. 18, No. 4, pp. 664-9.
Journal code: 8706402. ISSN: 0931-0509. L-ISSN: 0931-0509.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)

Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 16 Mar 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 25 Nov 2003

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record

AB BACKGROUND: During the development of non-infectious kidney stones, crystals form and deposit in the kidneys and become surrounded by monocytes/macrophages (M/M). We have proposed that in response to crystal exposure renal epithelial cells produce chemokines, which attract the M/M to the sites of crystal deposition. We investigated the expression of monocyte chemoattractant protein-1 (MCP-1) mRNA and protein by NRK52E rat renal tubular epithelial cells exposed to calcium oxalate (CaOx), brushite (Br, a calcium phosphate) and uric acid (UA) crystals.

METHODS: Confluent cultures of NRK52E cells were exposed to CaOx, Br or UA at a concentration of 250 micro g/ml (66.7 micro g/cm(2)). They were exposed for 1, 3, 6, 12, 24 and 48 h for isolation of mRNA and 24 h for ELISA to determine the secretion of protein into the culture medium. Since cells are known to produce free radicals on exposure to CaOx crystals we also investigated the effect of free radical scavenger catalase on the crystal induced expression of MCP-1 mRNA and protein.

RESULTS: Exposure of NRK52E cells to the crystals resulted in increased expression of MCP-1 mRNA and production of the chemoattractant. CaOx crystals were most provocative while UA the least. Treatment with catalase had a negative effect on the increased expression of both MCP-1 mRNA and protein, which indicates the involvement of free radicals in up-regulation of MCP-1 production.

CONCLUSION: Exposure to both CaOx and calcium phosphate crystals stimulates increased production of MCP-1. Free radicals appear to be involved in this up-regulation. Results indicate that MCP-1, which is often associated with localized inflammation, may be one of the chemokine mediators associated with the deposition of various urinary crystals in the kidneys during kidney stone formation. Because of the small number of experiments performed here, results must be confirmed by more extensive studies with larger sample size.

L2 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000258606 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10798271
TITLE: Endothelial function and hemostasis.
AUTHOR: Becker B F; Heindl B; Kupatt C; Zahler S
CORPORATE SOURCE: Dept. of Physiology, University of Munich, Germany.
SOURCE: Zeitschrift fur Kardiologie, (2000 Mar) Vol. 89,
No. 3, pp. 160-7. Ref: 54
Journal code: 0360430. ISSN: 0300-5860. L-ISSN: 0300-5860.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 6 Jun 2000
Last Updated on STN: 6 Jun 2000

Entered Medline: 25 May 2000

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
REFERENCE COUNT: 54 There are 54 cited references for this document.

AB The vascular endothelium influences not only the three classically interacting components of hemostasis: the vessel, the blood platelets and the clotting and fibrinolytic systems of plasma, but also the natural sequelae: inflammation and tissue repair. Two principal modes of endothelial behaviour may be differentiated, best defined as an anti- and a prothrombotic state. Under physiological conditions endothelium mediates vascular dilatation (formation of NO, PGI₂, adenosine, hyperpolarizing factor), prevents platelet adhesion and activation (production of adenosine, NO and PGI₂, removal of ADP), blocks thrombin formation (tissue factor pathway inhibitor, activation of protein C via thrombomodulin, activation of antithrombin III) and mitigates fibrin deposition (t- and scu-plasminogen activator production). Adhesion and transmigration of inflammatory leukocytes are attenuated, e.g. by NO and IL-10, and oxygen radicals are efficiently scavenged (urate, NO, glutathione, SOD). When the endothelium is physically disrupted or functionally perturbed by postischemic reperfusion, acute and chronic inflammation, atherosclerosis, diabetes and chronic arterial hypertension, then completely opposing actions pertain. This prothrombotic, proinflammatory state is characterised by vaso-constriction, platelet and leukocyte activation and adhesion (externalization, expression and upregulation of von Willebrand factor, platelet activating factor, P-selectin, ICAM-1, IL-8, MCP-1, TNF alpha, etc.), promotion of thrombin formation, coagulation and fibrin deposition at the vascular wall (expression of tissue factor, PAI-1, phosphatidyl serine, etc.) and, in platelet-leukocyte coaggregates, additional inflammatory interactions via attachment of platelet CD40-ligand to endothelial, monocyte and B-cell CD40. Since thrombin formation and inflammatory stimulation set the stage for later tissue repair, complete abolition of such endothelial responses cannot be the goal of clinical interventions aimed at limiting procoagulatory, prothrombotic actions of a dysfunctional vascular endothelium.

L2 ANSWER 8 OF 12 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1998377987 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9714185
TITLE: Production and regulation of monocyte chemoattractant protein-1 in lipopolysaccharide- or monosodium urate crystal-induced arthritis in rabbits: roles of tumor necrosis factor alpha, interleukin-1, and interleukin-8.
AUTHOR: Matsukawa A; Miyazaki S; Maeda T; Tanase S; Feng L; Ohkawara S; Yoshinaga M; Yoshimura T
CORPORATE SOURCE: Department of Pathology, Kumamoto University School of Medicine, Honjo, Japan.
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (1998 Aug) Vol. 78, No. 8, pp. 973-85.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal, Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 10 Sep 1998
Last Updated on STN: 10 Sep 1998
Entered Medline: 31 Aug 1998

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB The production of monocyte chemoattractant protein-1 (MCP-1) and its regulation by TNFalpha, IL-1, and IL-8 were

investigated in two rabbit models of arthritis induced by intra-articular injection of lipopolysaccharide (LPS) or monosodium urate (MSU) crystals. We first prepared recombinant rabbit MCP-1 and antibodies and then developed an immunoassay. The immunoassay detected 3 pg/ml rabbit MCP-1 and did not cross-react with other rabbit chemokines such as IL-8 or GRO. MCP-1 was first detected in synovial fluid (SF) at 1 hour, and peaked at 4 or 2 hours after the injection of LPS or MSU crystals, respectively. Immunohistochemically, MCP-1 was detected in synovial lining cells and infiltrating neutrophils. The amounts of MCP-1 detected in SF from neutrophil-depleted rabbits were similar to those in normal rabbits, suggesting that synovial lining cells were the main source of MCP-1 detected in SF. The peak level of MCP-1 in SF after LPS-injection was inhibited by 57% with anti-TNFalpha mAb and by 41% with IL-1 receptor antagonist (IL-1Ra). Coadministration of anti-TNFalpha mAb and IL-1Ra inhibited 90% of MCP-1 production. In contrast, the peak level of MCP-1 in SF after MSU crystal-injection was not affected by any cytokine inhibitor, but was reduced by 52% with coadministration of anti-TNFalpha mAb and IL-1Ra. Anti-IL-8 IgG had no effect on the production of MCP-1 in either model. Thus, the production of MCP-1 in LPS-induced arthritis was mostly regulated by TNFalpha and IL-1, whereas half the extent of MCP-1 production in MSU crystal-induced arthritis was independent of TNFalpha or IL-1. IL-8 does not seem to regulate the production of MCP-1 in SF either directly or indirectly. Finally, administration of neutralizing anti-MCP-1 antibody inhibited LPS- and MSU crystal-induced monocyte infiltration by 58.4% and 44.9%, respectively, suggesting that synovial production of MCP-1 plays an important role in the recruitment of monocytes in these arthritis models.

L2 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 9
 ACCESSION NUMBER: 1999338763 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10410574
 TITLE: [Soluble cell adhesion molecules in chronic renal graft rejection].
 Rozpuszczalne czasteczki adhezyjne w przewleklym odrzucaniu przeszczepionej nerki.
 AUTHOR: Boratynska M
 CORPORATE SOURCE: Katedra i Klinika Nefrologii, Akademii Medycznej we Wroclawiu.
 SOURCE: Polskie Archiwum Medycyny Wewnetrznej, (1998 Nov) Vol. 100, No. 5, pp. 410-8.
 Journal code: 0401225. ISSN: 0032-3772. L-ISSN: 0032-3772.
 PUB. COUNTRY: Poland
 DOCUMENT TYPE: (CLINICAL TRIAL)
 (CONTROLLED CLINICAL TRIAL)
 (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: Polish
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199908
 ENTRY DATE: Entered STN: 20 Aug 1999
 Last Updated on STN: 20 Aug 1999
 Entered Medline: 10 Aug 1999
 AB Cell-bound adhesion molecules are involved in immune and inflammatory responses. Soluble forms of adhesion molecules (s.a.m.) can be detected in the blood. The elevated blood levels of s.a.m. were found as a response to variety disease processes (e.g. septic shock, acute graft rejection, atherosclerosis). The objective of the present study was to measure the serum levels of s.a.m. in patients with chronic renal

allograft rejection and in recipients with a stable graft function. Evaluated was also the effect of activity of graft rejection (ch. g. r.) and risk factors of graft lesion on the levels of the investigated s.a.m. 34 patients with ch.g.r. were examined (Group I), 50 patients with a stable allograft function (Group II), and 25 healthy subjects (control). Group I patients were 76 +/- 34 months and Group II patients were 59 +/- 36 months after transplantation. Both groups of patients were treated with immunosuppressive drugs (CsA, azathioprine and prednisone) Group I patients had a higher plasma levels of creatinine and uric acid, increased arterial blood pressure and triglycerides concentrations, and lower plasma levels of HDL cholesterol, as compared to Group II patients. In all the examined subjects, serum concentrations of s.a.m. from the immunoglobulin and selectin families (s.ICAM-1, s.VCAM-1, s.E-selectin) were measured by the immunoenzymatic method. The investigations of s.a.m. in ch.g.r. patients revealed a statistically significant increase the serum levels of s.ICAM-1, s.VCAM-1 and s.E-selectin. Some disorders of the release of s.a.m. into blood were also found in patients without graft disfunction. In this patients were observed: increased levels of s.VCAM-1 and s.E-selectin. s.ICAM-1, s.VCAM-1 and s.E-selectin serum levels showed a correlation with plasma uric acid concentration and arterial pressure, whereas the other two molecules with the plasma level of triglycerides. Each of the three molecules had a negative correlation with the HDL cholesterol level. The regression analysis revealed a correlation of s.ICAM-1 and s.VCAM-1 with IL-6. The correlation of the molecules with chemokines (s.VCAM-1 and s. E-selectin with IL-8, and s. E-selectin with MCP-1) may results from their release in the course of the inflammatory process. The increased levels of circulating s.VCAM-1 and s.E-selectin found in renal allograft patients suggest a chronic stimulation and activation of the endothelium. Non-immunological mechanisms (such as arterial hypertension or metabolic disorders) contributed to the generation of the s.a.m. in patients with ch.g.r. and in those with stable graft function. The negative correlation of HDL with s.a.m. (s.ICAM-1, s.VCAM-1) suggests a protective role of HDL on the vascular endothelium by inhibiting the generation of these mediators.

L2 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:567151 BIOSIS
DOCUMENT NUMBER: PREV200200567151
TITLE: The regulation of inflammatory mediators by uric acid in vitro and in vivo, suggests a role for hyperuricemia in the pathogenesis of vascular disease.
AUTHOR(S): Kanellis, John [Reprint author]; Kang, Duk-Hee [Reprint author]; Nakagawa, Takahiko [Reprint author]; Watanabe, Susumu [Reprint author]; Li, Ping [Reprint author]; Mazzali, Marilda [Reprint author]; Ohashi, Ryuji [Reprint author]; Feng, Lili [Reprint author]; Johnson, Richard J. [Reprint author]
CORPORATE SOURCE: Division of Nephrology, Baylor College of Medicine, Houston, TX, USA
SOURCE: Journal of the American Society of Nephrology, (September, 2002) Vol. 13, No. Program and Abstracts Issue, pp. 60A. print.
Meeting Info.: Meeting of the American Society of Nephrology. Philadelphia, PA, USA. October 30-November 04, 2002. American Society of Nephrology.
CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002

Last Updated on STN: 7 Nov 2002

L2 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on
STN
ACCESSION NUMBER: 2001:177361 BIOSIS
DOCUMENT NUMBER: PREV200100177361
TITLE: Significance of monocyte chemoattractant protein-1 in human
atherosclerosis: Assessment in chronic hemodialysis.
AUTHOR(S): Kusano, Kengo F. [Reprint author]; Nakamura, Yoichi;
Nakamura, Kazufumi; Kusano, Hitoshi; Kusano, Isao; Ohe,
Tohru
CORPORATE SOURCE: Cardiovascular Medicine, Okayama University Medical School,
Okayama, Japan
SOURCE: Journal of the American College of Cardiology, (
February, 2001) Vol. 37, No. 2 Supplement A, pp.
288A. print.
Meeting Info.: 50th Annual Scientific Session of the
American College of Cardiology. Orlando, Florida, USA.
March 18-21, 2001. American College of Cardiology.
CODEN: JACCDI. ISSN: 0735-1097.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Apr 2001
Last Updated on STN: 18 Feb 2002

L2 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2001:922560 CAPLUS
DOCUMENT NUMBER: 136:293252
TITLE: Differential production of RANTES and MCP-1 in
synovial fluid from the inflamed human knee
AUTHOR(S): Conti, Pio; Reale, Marcella; Barbacane, Renato C.;
Castellani, Maria Luisa; Orso, Claudio
CORPORATE SOURCE: Immunology Division, University of Chieti School of
Medicine, Chieti, 66013, Italy
SOURCE: Immunology Letters (2002), 80(2), 105-111
CODEN: IMLED6; ISSN: 0165-2478
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Synovial production of chemokines may play an important role in the
recruitment of phagocytic leukocytes during inflammation. MCP-1, as well
as RANTES mediate many different inflammatory diseases and are important
in the recruitment of diverse leukocytes. The authors set out to study
the different production of MCP-1 and RANTES in three different inflammatory
conditions of the knee: arthrosynovitis, mech. trauma, and hyperuricemia.
In this study the authors evaluated if in each pathol. condition mentioned
above, there was a prevalence in production of one chemokine over the other.
ELISA method was used to determine base production of the chemokines in the
synovial fluid, serum and in supernatants from activated inflammatory
cells. RANTES and MCP-1 mRNA was measured by semi-quant. RT-PCR. Protein
expression was detected by Western blot anal. The synovial fluid cells
from the knee of patients affected with arthrosynovitis, trauma, and
hyperuricemia, expressed RANTES and MCP-1 and RANTES was produced in
higher quantities than MCP-1 in all three pathol. conditions. In patients
treated with non-steroidal antiinflammatory drugs (NSAID) and
dexamethasone, the levels of the two chemokines was reduced in serum and
in synovial fluid. In addition, the synovial fluid cells from these patients
released less RANTES and MCP-1 when compared to untreated patients. The
authors conclude that in arthrosynovitis, trauma and hyperuricemia, RANTES
and MCP-1 are both expressed and RANTES is produced in higher quantities.
The fact that these chemokines are found in the three inflammatory

diseases suggests that RANTES and MCP-1 are not specific to these inflammatory diseases, however they play a key role in inflammation by recruiting mononuclear leukocytes in the inflamed knee joint.

OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS 15 DEC 22 Value-Added Indexing Improves Access to World Traditional Medicine Patents in CAPLUS
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=> S (Thymidine incorporation)(S) Proliferation (S) assay AND pd<=20041111
L1 1378 (THYMIDINE INCORPORATION)(S) PROLIFERATION (S) ASSAY AND PD<=20041111

=> Dup Rem l1
PROCESSING IS APPROXIMATELY 50% COMPLETE FOR L1
PROCESSING COMPLETED FOR L1
L2 463 DUP REM L1 (915 DUPLICATES REMOVED)
ANSWERS '1-371' FROM FILE MEDLINE
ANSWERS '372-415' FROM FILE BIOSIS
ANSWERS '416-454' FROM FILE CAPLUS
ANSWERS '455-463' FROM FILE EMBASE

=> S L2 AND review
L3 5 L2 AND REVIEW

=> Dup rem L3
PROCESSING COMPLETED FOR L3
L4 5 DUP REM L3 (0 DUPLICATES REMOVED)
ANSWER '1' FROM FILE MEDLINE
ANSWERS '2-5' FROM FILE CAPLUS

=> D ibib abs L4

L4 ANSWER 1 OF 5 MEDLINE on STN
ACCESSION NUMBER: 1987279417 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3112053
TITLE: AIDS studies in Japan.
AUTHOR: Harada S; Yamamoto N
SOURCE: Japanese journal of cancer research : Gann, (1987
May) Vol. 78, No. 5, pp. 415-27. Ref: 88
Journal code: 8509412. ISSN: 0910-5050. L-ISSN: 0910-5050.
Report No.: PIP-061952; POP-00198952.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population; AIDS
ENTRY MONTH: 198709
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 10 Sep 1987
REFERENCE COUNT: 88 There are 88 cited references for this document.
AB The AIDS Surveillance System in Japan was set up in 1984 and by 1987, 29
AIDS patients had been reported. 10 were homosexuals, 16 were hemophiliacs
and 3 were heterosexuals. 9 out of 16 hemophiliacs with AIDS had A-type
hemophilia. 2 females were also reported as victims of AIDS. 19 patients
have died 5 male homosexuals (4.4%) out of 113 (93 Japanese and 20
Foreigners) individuals were anti-HIV-positive. In 1984 sera from 65
hemophiliacs, 85 hemodialysis patients and 304 healthy volunteer blood
donors were examined and 10 (15.4%) of the hemophiliacs proved to be
anti-HIV positive. On the other hand, in Tokyo and Nagasaki 50-60% were
positive, but in Tottori and Osaka only 25-28% were positive. The
enzyme-linked immunosorbent assay (ELISA) test is widely used to detect
antibodies, however, the test often gives false-positive reactions, and
the blood must be reexamined by means of the Western-blot test or IF
method. Therefore, a simple particle agglutination (FA) assay was
developed by the authors using gelatin beads as the artificial antigen
carrier. This assay is extremely sensitive as compared to IF and ELISA.
Among HTLV-1/ATLV-carrying T-cell lines, all except one (TCL-As) were
susceptible to HIV infection and showed cytopathic effect (CPE). HIV has
quite a broad host range in vivo and in vitro. HIV was detected in brain
macrophages from AIDS patients with encephalopathy. HIV may also infect
nerve cells or glial cells. The MT-4 cell line was found to be most prone
to HIV infection. In order to evaluate the virus-induced CPE of infected
MT-4 cells, the H-thymidine incorporation method (cell
proliferation assay) was developed that involved that
involves measuring the survival of the cells. Inhibition of DNA synthesis
in infected MT-4 cells was detected by this assay when the CPE was
observed microscopically. This assay system is also useful for measuring
the amount of infectious virus. Many chemico-physical agents such as
suramin, antimoniotungstate (HFA-23), phosphonoformic acid, ribavirin,
3-azido-3-deoxythymidine (AZT) have suppressive effects on the replication
of HIV in vitro. Glycyrrhizin administration was responsible for
improvement of immune function in 6 of 7 asymptomatic HIV carriers.
Prostaglandin E2 (PGE2) and 12-O-tetradecanoylphorbol-13- acetate (TPA)
were found to enhance the production of HIV significantly in infected MT-4
cells. The cell proliferation assay is used for the mass screening of
neutralizing antibodies whose presence in the sera from 21 patients with
AIDS, 10 individuals with ARC, 20 healthy male homosexuals and 10 healthy
males was examined. The assay was sensitive enough to detect neutralizing
antibodies up to a dilution of 1:10 thousand. The system using MT-4 cells
seems to be suited for this purpose.

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L1      1378 S (THYMIDINE INCORPORATION)(S) PROLIFERATION (S) ASSAY AND PD<=
L2      463 DUP REM L1 (915 DUPLICATES REMOVED)
L3      5 S L2 AND REVIEW
L4      5 DUP REM L3 (0 DUPLICATES REMOVED)
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FILE 'STNGUIDE' ENTERED AT 11:44:09 ON 03 FEB 2011

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=> File .Gerry2mbce
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                                ENTRY      SESSION
FULL ESTIMATED COST          0.32      21.26
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FILE 'MEDLINE' ENTERED AT 11:47:10 ON 03 FEB 2011

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=> Dup rem l2
PROCESSING COMPLETED FOR L2
L5 463 DUP REM L2 (0 DUPLICATES REMOVED)
ANSWERS '1-371' FROM FILE MEDLINE
ANSWERS '372-415' FROM FILE BIOSIS
ANSWERS '416-454' FROM FILE CAPLUS
ANSWERS '455-463' FROM FILE EMBASE

=> S L5 AND method
L6 188 L5 AND METHOD

=> Dup rem l6
PROCESSING COMPLETED FOR L6
L7 188 DUP REM L6 (0 DUPLICATES REMOVED)
ANSWERS '1-139' FROM FILE MEDLINE
ANSWERS '140-171' FROM FILE BIOSIS
ANSWERS '172-182' FROM FILE CAPLUS
ANSWERS '183-188' FROM FILE EMBASE

=> D Ibib Abs L7 1-139

L7 ANSWER 1 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004558466 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15476280
TITLE: Pancreatic carcinoma cells express neuropilins and vascular endothelial growth factor, but not vascular endothelial growth factor receptors.
AUTHOR: Li Min; Yang Hui; Chai Hong; Fisher William E; Wang Xiaoping; Brunicardi F Charles; Yao Qizhi; Chen Changyi
CORPORATE SOURCE: Molecular Surgeon Research Center, Michael E. DeBakey Department of Surgery, Baylor College of Medicine/Methodist Hospital, Houston, Texas 77030, USA.
CONTRACT NUMBER: K08 CA85822 (United States NCI NIH HHS)
R01 CA95731 (United States NCI NIH HHS)
R01 DE015543 (United States NIDCR NIH HHS)
R01 DK46441 (United States NIDDK NIH HHS)
R01 HL60135 (United States NHLBI NIH HHS)
R01 HL61943 (United States NHLBI NIH HHS)
R01 HL65916 (United States NHLBI NIH HHS)
R01 HL72716 (United States NHLBI NIH HHS)
R13 CA101889 (United States NCI NIH HHS)
R21 AI49116 (United States NIAID NIH HHS)
SOURCE: Cancer, (2004 Nov 15) Vol. 101, No. 10, pp. 2341-50.
Journal code: 0374236. ISSN: 0008-543X. L-ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 9 Nov 2004
Last Updated on STN: 23 Dec 2004
Entered Medline: 22 Dec 2004
OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB BACKGROUND: Neuropilins (NRPs) are characterized as coreceptors of vascular endothelial growth factor (VEGF). In the current study, the authors assessed the expression of NRPs, VEGF, and vascular endothelial growth factor receptors (VEGFRs), as well as VEGF-induced cell

proliferation, in pancreatic carcinoma cell lines and tissue specimens.

METHODS: Human pancreatic carcinoma cell lines (Panc-1 and MIA PaCa-2), normal human pancreatic ductal epithelial cells (HPDE), and human umbilical vein endothelial cells (HUVECs) were cultured. Human pancreatic adenocarcinoma tissue specimens were also studied. Expression levels of NRPs, VEGFRs, and VEGF were determined by real-time polymerase chain reaction analysis and immunostaining. Cell proliferation was examined using a [3H]thymidine incorporation assay.

RESULTS: Both NRP-1 and NRP-2 were expressed in Panc-1 cells, HPDE cells, and HUVECs but were expressed minimally in MIA PaCa-2 cells. Panc-1 expressed 30 times more NRP-1 mRNA than NRP-2 mRNA. NRP-1 levels in Panc-1 cells were 5.3 times higher than in HPDE cells but were similar to NRP-1 levels in HUVECs. NRP-2 levels in Panc-1 cells were similar to NRP-2 levels in HPDE cells but lower than NRP-2 levels in HUVECs. Expression of all three VEGFRs was observed only in HUVECs. However, VEGF mRNA was detected in all cell types except for HUVECs. NRP-1 immunoreactivity levels were much higher than NRP-2 immunoreactivity levels in Panc-1 and human pancreatic adenocarcinoma tissue specimens, whereas VEGFRs were not detected in either of these two settings. In response to VEGF165, [3H]thymidine incorporation in Panc-1 cells increased significantly (by 61%; $P < 0.01$). A monoclonal antibody against human NRP-1 significantly blocked VEGF-induced cell proliferation in Panc-1 cells.

CONCLUSIONS: The pancreatic carcinoma cell line Panc-1 and adenocarcinoma tissue specimens expressed high levels of NRP-1 and VEGF, but not VEGFRs, and exogenous VEGF significantly increased NRP-1-mediated, but not VEGFR-mediated, Panc-1 cell proliferation. These data suggested that NRP-1 may be involved in the pathogenesis of pancreatic carcinoma.
(c) 2004 American Cancer Society

L7 ANSWER 2 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004595487 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15569414
TITLE: Immunoenhancing activity of protopanaxatriol-type ginsenoside-F3 in murine spleen cells.
AUTHOR: Yu Jun-li; Dou De-qiang; Chen Xiao-hong; Yang Hong-zhen; Guo Na; Cheng Gui-fang
CORPORATE SOURCE: Department of Pharmacology, Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing 100050, China.
SOURCE: Acta pharmacologica Sinica, (2004 Dec) Vol. 25, No. 12, pp. 1671-6. Journal code: 100956087. ISSN: 1671-4083. L-ISSN: 1671-4083.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 1 Dec 2004
Last Updated on STN: 25 Jun 2005
Entered Medline: 24 Jun 2005
AB AIM: To investigate the immunoenhancing activity of ginsenoside-F3 in murine spleen cells and explore its mechanism.

METHODS: The enhancing effect of ginsenoside-F3 on murine spleen cell proliferation was studied using [3H]

thymidine incorporation assay. Effects of ginsenoside-F3 on the production of type 1 cytokines IL-2, IFN-gamma, and type 2 cytokines IL-4 and IL-10 from murine spleen cells were detected by ELISA method. Effects of ginsenoside-F3 on mRNA level of cytokines IL-4, IFN-gamma, and transcription factors T-bet and GATA-3 were evaluated by RT-PCR analysis. Effect of ginsenoside-F3 on NF-kappaB DNA binding activity in murine spleen cells was investigated by electrophoretic mobility shift assays (EMSA).

RESULTS: Ginsenoside-F3 at 0.1-100 micromol/L not only promoted the murine spleen cell proliferation, but also increased the production of IL-2 and IFN-gamma, while decreased the production of IL-4 and IL-10 from murine spleen cells with the maximal effect at 10 micromol/L. RT-PCR analysis displayed that ginsenoside-F3 enhanced the IFN-gamma and T-bet gene expression and decreased IL-4 and GATA-3 gene expression. EMSA experiment showed that ginsenoside-F3 10 micromol/L enhanced the NF-kappaB DNA binding activity induced by ConA in murine spleen cells.

CONCLUSION: Ginsenoside-F3 has immunoenhancing activity by regulating production and gene expression of type 1 cytokines and type 2 cytokines in murine spleen cells.

L7 ANSWER 3 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004318798 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15178657
TITLE: Proliferation of ovarian theca-interstitial cells is modulated by antioxidants and oxidative stress.
AUTHOR: Duleba A J; Foyouzi N; Karaca M; Pehlivan T; Kwintkiewicz J; Behrman H R
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, CT 06510, USA. antoni.duleba@yale.edu
CONTRACT NUMBER: R01 HD40207 (United States NICHD NIH HHS)
SOURCE: Human reproduction (Oxford, England), (2004 Jul) Vol. 19, No. 7, pp. 1519-24. Electronic Publication: 2004-06-03. Journal code: 8701199. ISSN: 0268-1161. L-ISSN: 0268-1161.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 29 Jun 2004
Last Updated on STN: 14 Jan 2005
Entered Medline: 13 Jan 2005
OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB BACKGROUND: Maintenance of ovarian homeostasis requires precise regulation of proliferation of thecal- interstitial (T-I) cells. Recent evidence indicates that oxidative stress and antioxidants modulate proliferation of various tissues under both physiological and pathological conditions. This study evaluated the effects of oxidative stress and antioxidants on T-I proliferation.

METHODS: Rat T-I cells were cultured in serum-free medium and proliferation was assessed by determination of DNA synthesis using the thymidine incorporation assay, by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay and by direct counting of steroidogenically active cells and steroidogenically inactive cells.

RESULTS: Antioxidants and reactive oxygen scavengers induced a

dose-dependent decrease of T-I proliferation. Vitamin E succinate was inhibitory at 10-100 micro mol/l, ebselen was inhibitory at 0.3-30 micro mol/l, and superoxide dismutase was inhibitory at 300-1000 IU/ml. In contrast, oxidative stress resulted in a biphasic effect. Modest oxidative stress induced by 1 mmol/l hypoxanthine and xanthine oxidase (3-30 micro U/ml) stimulated proliferation of T-I cells, while greater oxidative stress induced by xanthine oxidase (1 mU/ml) profoundly inhibited proliferation. Direct cell counting demonstrated comparable effects on steroidogenically active and inactive cells.

CONCLUSIONS: Reactive oxygen species may play a role in the regulation of growth of ovarian mesenchyme. Under pathological conditions, such as those encountered in polycystic ovary syndrome, excessive oxidative stress and depletion of antioxidants may contribute to ovarian mesenchymal hyperplasia.

L7 ANSWER 4 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004543713 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15515342
TITLE: Platelet-released supernatant increases matrix metalloproteinase-2 production, migration, proliferation, and tube formation of human umbilical vascular endothelial cells.
AUTHOR: Kandler Barbara; Fischer Michael B; Watzek Georg; Gruber Reinhard
CORPORATE SOURCE: Dental School, Department of Oral Surgery, Medical University of Vienna, Vienna, Austria.
SOURCE: Journal of periodontology, (2004 Sep) Vol. 75, No. 9, pp. 1255-61.
JOURNAL CODE: 8000345. ISSN: 0022-3492. L-ISSN: 0022-3492.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 2 Nov 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 2 Dec 2004
AB BACKGROUND: Local application of platelets represents a promising tool to enhance bone regeneration. New bone formation strictly requires blood vessel formation, a sequential process involving matrix degradation, migration, proliferation, and tube formation of endothelial cells. Here we investigated the impact of secreted granula products from activated platelets on endothelial cells, and determined the involvement of extracellular signal-regulated kinase (ERK) signaling.
METHODS: The effects of platelet-released supernatant on endothelial cells were investigated using in vitro models. Matrix metalloproteinase-2 (MMP-2) release, migration, proliferation, and tube formation of human umbilical vascular endothelial cells (HUVEC) were determined in response to platelet-released supernatant by gelatine zymography, Boyden chamber assay, 3[H]thymidine incorporation, and basement membrane assay, respectively. All experiments were performed in the presence of the ERK signaling inhibitor PD98059. ERK phosphorylation was detected by Western blot analysis.
RESULTS: Incubation with platelet-released supernatant increased the production of MMP-2, migration, proliferation, and tube formation of HUVEC. Platelet-released supernatant also stimulated ERK phosphorylation in HUVEC. Inhibition of ERK signaling decreased platelet-released

supernatant-stimulated endothelial cell proliferation, but not MMP-2 activity, migration, and the formation of capillary tubes.

CONCLUSIONS: Our data suggest that secreted granula products from platelets can enhance different stages of blood vessel formation, and that ERK signaling is required to mediate the mitogenic effects of the supernatant. These findings support the hypothesis of a potential link between platelet activation and blood vessel formation during bone regeneration.

L7 ANSWER 5 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004318467 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15164168
TITLE: Potent activation of multiple signalling pathways by C-peptide in opossum kidney proximal tubular cells.
AUTHOR: Al-Rasheed N M; Meakin F; Royal E L; Lewington A J; Brown J; Willars G B; Brunskill N J
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, Faculty of Medicine and Biological Sciences, University of Leicester, Medical Sciences Building, University Road, Leicester LE1 9HN, United Kingdom.
SOURCE: Diabetologia, (2004 Jun) Vol. 47, No. 6, pp. 987-97. Electronic Publication: 2004-05-26. Journal code: 0006777. ISSN: 0012-186X. L-ISSN: 0012-186X. Germany: Germany, Federal Republic of
PUB. COUNTRY: Germany; Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 29 Jun 2004
Last Updated on STN: 16 Feb 2005
Entered Medline: 15 Feb 2005

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB AIMS/HYPOTHESIS: Proinsulin C-peptide is generally believed to be inert without any appreciable biological functions. However, it has been shown to modulate a variety of cellular processes important in the pathophysiology of diabetic complications. We therefore investigated the ability of C-peptide to stimulate intracellular signalling pathways in kidney proximal tubular cells, the altered activation of which may possibly be related to the development of diabetic nephropathy.

METHODS: Extracellular signal-regulated kinase (ERK) and Akt phosphorylation were evaluated by western blotting. ERK activity was measured by in vitro kinase assay. Intracellular Ca(2+) was evaluated by confocal imaging. The membrane and cytosol-associated fractions of protein kinase C (PKC) isoforms were evaluated by western blotting. Proliferation was assessed by thymidine incorporation assay.

RESULTS: Using the opossum proximal tubular kidney cell line as a model, we demonstrated that at high picomolar to low nanomolar concentrations, C-peptide stimulates extracellular signal-regulated mitogen-activated kinase (3.3+/-0.1-fold over basal at 3 minutes) and phosphatidylinositol 3-kinase (4.1+/-0.05-fold over basal at 5 minutes). ERK activation was attenuated by pre-treatment with a PKC inhibitor and abolished by pertussis toxin. Elevations of intracellular [Ca(2+)] are seen in response to 5 nmol/l C-peptide with consequent activation of PKC-alpha. Pre-treatment with pertussis toxin abolished PKC-alpha. C-peptide is also a functional mitogen in this cell type, stimulating significantly increased cell proliferation. Proliferation was attenuated by wortmannin and pertussis toxin pre-treatments. None of these effects is reproduced

by scrambled C-peptide.

CONCLUSIONS/INTERPRETATION: This study provides evidence that C-peptide, within physiological concentration ranges, stimulates many signalling pathways in opossum kidney cells.

L7 ANSWER 6 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004444199 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15351544
TITLE: Individual susceptibility to hexavalent chromium of workers of shoe, hide, and leather industries. Immunological pattern of HLA-B8, DR3-positive subjects.
AUTHOR: Mignini Fiorenzo; Streccioni Valentino; Baldo Meris; Vitali Mario; Indraccolo Ugo; Bernacchia Gianna; Cocchioni Mario
CORPORATE SOURCE: Sezione di Anatomia Umana-Dipartimento di Scienze Farmacologiche e Medicina Sperimentale, via M. Scalzino no. 3, Universita di Camerino, 62032, Italy.
SOURCE: fiorenzo.mignini@unicam.it
Preventive medicine, (2004 Oct) Vol. 39, No. 4, pp. 767-75.
JOURNAL CODE: 0322116. ISSN: 0091-7435. L-ISSN: 0091-7435.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 8 Sep 2004
Last Updated on STN: 19 Apr 2005
Entered Medline: 18 Apr 2005
AB BACKGROUND: This study was designed to examine the effects of hexavalent chromium [Cr(VI)] on the immunological pattern of shoe, hide, and leather industry workers, moving from the hypothesis that some haplotypes (HLA-B8,DR3) can be important hidden risk cofactors.

METHODS: Workplaces of 20 firms were monitored for total and respirable dusts and for total and hexavalent chromium. Cr(VI) on materials was also measured. Assay of chromium levels in blood and urine of 44 serological human leukocytes antigen (HLA)-typed workers (20 exposed, 15 HLA-B8,DR3-negative/5-positive and 24 non-exposed, 18 HLA-B8,DR3-negative/6-positive subjects) was performed by atomic absorption, and lymphocyte subsets (FACS-analysis), mitogen-mediate lympho-proliferation ([3H]thymidine incorporation), cytokine levels (ELISA), natural killer (NK) cytotoxic activity (51Cr-release assay) were determined.

RESULTS: The environmental parameter levels are lower than threshold limit value-time-weighted average (TLV-TWA); in the materials, the Cr(VI) values exceeded the levels allowed. The peripheral blood mononuclear cells (PBMC) proliferation and the T-helper1 (TH1) cytokine pattern of subjects chronically exposed were significantly raised; addition in vitro of Cr(VI) further stimulated these parameters and in general the entire TH1 system and NK activity. The TH2 system was unaltered. In the HLA-B8,DR3-positive workers, immunologically "low responders", the addition of Cr(VI) in vitro caused a further reduction of the considered parameters in the exposed subjects with a dramatic deficit of the TH1 system.

CONCLUSIONS: Results indicate the unsuitability of TLV-TWA as a line of demarcation between safe and dangerous Cr(VI) concentrations and the importance of individual genetic susceptibility for occupational and

preventative medicine. In particular, the presence of the HLA-B8,DR3 alleles can represent an important cofactor of immunotoxic susceptibility consequent to chronic low-dose Cr(VI) exposure.

L7 ANSWER 7 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004069721 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14872508
TITLE: Induction of costimulation of human CD4 T cells by tumor necrosis factor-related apoptosis-inducing ligand: possible role in T cell activation in systemic lupus erythematosus.
AUTHOR: Tsai Hwei-Fang; Lai Jiann-Jyh; Chou Ai-Hsiang; Wang Ting-Fang; Wu Chien-Sheng; Hsu Ping-Ning
CORPORATE SOURCE: College of Medicine, National Taiwan University, and Taipei Ho-Ping Municipal Hospital, Taipei, Taiwan, Republic of China.
SOURCE: Arthritis and rheumatism, (2004 Feb) Vol. 50, No. 2, pp. 629-39.
JOURNAL CODE: 0370605. ISSN: 0004-3591. L-ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 12 Feb 2004
Last Updated on STN: 3 Mar 2004
Entered Medline: 2 Mar 2004
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB OBJECTIVE: Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) has recently been shown to induce costimulation of mouse T cells in conjunction with signals from the T cell receptor. This study was undertaken to investigate TRAIL-induced costimulation of human T cells in order to determine the role of TRAIL-induced T cell activation in human systemic lupus erythematosus (SLE).
METHODS: An in vitro T cell stimulation system with immobilized anti-CD3 and recombinant TRAIL receptor DR4-Fc proteins was used to activate human T cells purified from healthy individuals and from patients with SLE. The T cells were stimulated in vitro to assay their proliferation response by (3)H-thymidine incorporation, and their cytokine production by enzyme-linked immunosorbent assay. Activation of p38 MAPK after TRAIL stimulation was detected with specific anti-phospho-p38 MAPK monoclonal antibodies in Western blots.
RESULTS: Enhanced T cell proliferation and increased interleukin-2 and interferon-gamma (IFNgamma) production were demonstrated in human T cells after stimulation with immobilized DR4-Fc and anti-CD3 in vitro. TRAIL engagement selectively activated human CD4, rather than CD8, T cells and augmented IFNgamma production. Activation of p38 MAPK was detected after TRAIL-induced T cell activation. T cells isolated from patients with SLE demonstrated a stronger response to TRAIL-induced costimulation, in terms of proliferation and increased up-regulation of CD25 after activation, when compared with T cells from healthy subjects.
CONCLUSION: TRAIL engagement induces costimulation of human CD4 T cells via a p38 MAPK-dependent pathway. The results suggest that enhanced reactivity of T cells to autoantigens as a result of TRAIL-induced costimulation may play a role in the development of human autoimmune diseases.

L7 ANSWER 8 OF 188 MEDLINE on STN

ACCESSION NUMBER: 2004351062 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15253857
TITLE: Yin zi huang, an injectable multicomponent chinese herbal medicine, is a potent inhibitor of T-cell activation.
AUTHOR: Chen Xin; Krakauer Teresa; Oppenheim Joost J; Howard O M Zack
CORPORATE SOURCE: Basic Research Program, SAIC-Frederick, Inc., National Cancer Institute-Frederick, Frederick, MD 21702-1201, USA.
CONTRACT NUMBER: N01-CO-12400 (United States NCI NIH HHS)
SOURCE: Journal of alternative and complementary medicine (New York, N.Y.), (2004 Jun) Vol. 10, No. 3, pp. 519-26.
Journal code: 9508124. ISSN: 1075-5535. L-ISSN: 1075-5535.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 16 Jul 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 19 Nov 2004

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB OBJECTIVES: The clinical efficacy of many multiherbal Traditional Chinese Medicines (TCM) is partially attributable to their immunoregulatory properties. In this study we evaluated the effect of eight commonly used, commercially available multiherbal Chinese medicines on T-cell activation. We focused on Yin Zhi Huang (YZH, an injectable herbal medicine commonly used for the treatment of liver diseases in China), because it was the most potent inhibitor of T-cell activation in our experimental system. The effects of 10 ingredient components of YZH were also evaluated.

METHODS: [3H] thymidine incorporation assay was used to assess mouse T-cell proliferation after stimulation with latex beads coated with anti-CD3/CD28 antibodies. CD25, CD69, PD-1, and I-COS expression by purified mouse CD4+ T cells treated with plate-bound anti-CD3 antibody and soluble anti-CD28 antibody was analyzed by fluorescent-activated cell sorter (FACS). Cytokine/chemokine production by human peripheral blood mononuclear cells (PBMC) stimulated with staphylococcal enterotoxin B (SEB) was determined by enzyme-linked immunosorbent assay (ELISA).

RESULTS: Among tested herbal medicines, YZH was the most potent inhibitor of T-cell activation. In splenocyte proliferation assays, the inhibitory effect of YZH was dose-dependent, with a 50% inhibition concentration (IC50) of 1:3200-1:1600. Ten (10) purified compounds found in YZH were evaluated for their activity. Among them, ursolic acid (1-10 micromol), luteolin (1-10 micromol), baicalein (1-10 micromol), scopran (5-50 micromol), and crocin (5-50 micromol), exhibited dose-dependent inhibition. YZH also inhibited CD25, CD69, PD-1, and ICOS expression by stimulated mouse CD4+ T cells. In human PBMCs, YZH inhibited SEB-stimulated cytokine (interleukin [IL]-1, IL-2, IL-6, tumor necrosis factor [TNF]-alpha, interferon [IFN]-gamma) and chemokine (IP-10, MCP-1, MIP-1alpha and MIP-1beta) production in a dose-dependent manner.

CONCLUSION: Our data show for the first time that YZH is a potent inhibitor of T-cell activation, and this property may be the major mechanism underlying the clinical efficacy of YZH. Our experimental results pave the way for identification of active component(s) and/or analysis of synergistic/additive effect of a YZH ingredient in future studies.

L7 ANSWER 9 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004160424 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14762654
TITLE: Glucagon-like peptide-1 regulates proliferation and apoptosis via activation of protein kinase B in pancreatic INS-1 beta cells.
AUTHOR: Wang Q; Li L; Xu E; Wong V; Rhodes C; Brubaker P L
CORPORATE SOURCE: Department of Physiology, University of Toronto, Toronto, Ontario, Canada.
SOURCE: Diabetologia, (2004 Mar) Vol. 47, No. 3, pp. 478-87. Electronic Publication: 2004-02-05.
JOURNAL CODE: 0006777. ISSN: 0012-186X. L-ISSN: 0012-186X.
PUB. COUNTRY: Germany; Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 1 Apr 2004
Last Updated on STN: 23 Dec 2004
Entered Medline: 22 Dec 2004

OS.CITING REF COUNT: 14 There are 14 MEDLINE records that cite this record
AB AIMS/HYPOTHESIS: The incretin hormone glucagon-like peptide-1 augments islet cell mass in vivo by increasing proliferation and decreasing apoptosis of the beta cells. However, the signalling pathways that mediate these effects are mostly unknown. Using a clonal rat pancreatic beta cell line (INS-1), we examined the role of protein kinase B in mediating beta-cell growth and survival stimulated by glucagon-like peptide-1.

METHODS: Immunoblot analysis was used to detect active (phospho-) and total protein kinase B. Proliferation was assessed using (3)H-thymidine incorporation, while apoptosis was quantitated using 4'-6-diamidino-2-phenylindole staining and APO percentage apoptosis assay. Kinase-dead and wild-type protein kinase B was introduced into cells using adenoviral vectors.

RESULTS: Glucagon-like peptide-1 rapidly activated protein kinase B in INS-1 cells (by 2.7+/-0.7-fold, $p<0.05$). This effect was completely abrogated by inhibition, with wortmannin, of the upstream activator of protein kinase B, phosphatidylinositol-3-kinase. Glucagon-like peptide-1 also stimulated INS-1 cell proliferation in a dose-dependent manner (by 1.8+/-0.5-fold at $10(-7)$ mol/L, $p<0.01$), and inhibited staurosporine-induced apoptosis (by 69+/-12%, $p<0.05$). Both of these effects were also prevented by wortmannin treatment. Ablation of protein kinase B by adenovirus-mediated overexpression of the kinase-dead form of protein kinase B prevented protein kinase B phosphorylation and completely abrogated both cellular proliferation ($p<0.05$) and protection from drug-induced cellular death ($p<0.01$) induced by glucagon-like peptide-1.

CONCLUSIONS/INTERPRETATION: These results identify protein kinase B as an essential mediator linking the glucagon-like peptide-1 signal to the intracellular machinery that modulates beta-cell growth and survival.

L7 ANSWER 10 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004366764 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15268804
TITLE: Effects of growth factors and extracellular matrix on proliferation and differentiation of fetal liver progenitor

cell in vitro.
AUTHOR: Qin Ai-Lan; Zhou Xia-Qiu; Yu Hong; Xie Qing; Zhang Wei; Guo Qing
CORPORATE SOURCE: Laboratory of Severe Liver Diseases, Rui Jin Hospital
Affiliated to Shanghai Second Medical University, Shanghai
200025, China.
SOURCE: Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi
= Chinese journal of hepatology, (2004 Jul) Vol.
12, No. 7, pp. 406-9.
Journal code: 9/10009. ISSN: 1007-3418. L-ISSN: 1007-3418.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 23 Jul 2004
Last Updated on STN: 23 Apr 2005
Entered Medline: 22 Apr 2005

AB OBJECTIVE: Liver development needs a number of growth factors and components of the extracellular matrix. The study is to explore how growth factors and extracellular matrix regulate proliferation and differentiation of fetal liver progenitor cell.

METHODS: We demonstrate isolation of hepatic progenitor/stem cells from ED 14.5 SD rat liver, which contains a large number of hepatoblasts. Proliferation assay-3H thymidine incorporation was used to detect the effect of growth factors on proliferation of hepatic progenitor cell. Growth factor and extracellular matrix were added and stem cell clone formation was counted. Mark of bile duct and hepatocyte were detected with double-marker immunocytochemistry.

RESULTS: Progenitor liver cells displayed clonogenic capacity, expressed markers of hepatocytes and bile duct cells and G-6-P. HGF, EGF can accelerate DNA synthesis and stem cell clone formation of hepatic progenitor cell. Extracellular matrix collagen I, collagen IV or laminin were essential for formation of stem cell clone. Single cell culture needed HGF, EGF, extracellular matrix and supernatant of mix cell (which contained fetal parenchymal cells, mesenchymal cells and hematopoietic cells) culture.

CONCLUSION: Growth factors especially HGF and EGF play crucial role in proliferation and differentiation of liver progenitor cell. Some factors secreted from mesenchymal cell and hematopoietic cells may be involved.

L7 ANSWER 11 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004101012 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14991903
TITLE: Vascular endothelial growth factor (VEGF) induces matrix metalloproteinase expression in immortalized chondrocytes.
AUTHOR: Pufe Thomas; Harde Viola; Petersen Wolf; Goldring Mary B; Tillmann Bernhard; Mentlein Rolf
CORPORATE SOURCE: Department of Anatomy, University of Kiel, D-24098 Kiel, Germany.
CONTRACT NUMBER: AG22021 (United States NIA NIH HHS)
AR45378 (United States NIAMS NIH HHS)
SOURCE: The Journal of pathology, (2004 Mar) Vol. 202,
No. 3, pp. 367-74.
Journal code: 0204634. ISSN: 0022-3417. L-ISSN: 0022-3417.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 2 Mar 2004
Last Updated on STN: 17 Apr 2004
Entered Medline: 16 Apr 2004

OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record
AB VEGF (vascular endothelial growth factor), an important angiogenesis factor, appears also to be involved in inflammatory processes. Recent studies have shown that VEGF and its receptors (VEGFR) are expressed on osteoarthritic, but not on normal adult, chondrocytes. To elucidate possible functions of VEGF in osteoarthritic cartilage, the effects of VEGF were studied on immortalized human chondrocytes. Activated matrix metalloproteinase (MMP)-1, MMP-3, MMP-13, tissue inhibitor of metalloproteinases (TIMP)-1, TIMP-2, interleukin (IL)-1beta, IL-6, and tumour necrosis factor-alpha (TNF-alpha) were measured in culture supernatants by enzyme-linked immunosorbent assays, nitric oxide with the Griess reagent, and cell proliferation by [3H] thymidine incorporation. VEGFR-2 mRNA was quantified by real-time reverse transcription-polymerase chain reaction and the protein was identified by immuno-gold electron microscopy. Intracellular signal transduction effects were determined by western blots and electrophoretic mobility shift assays. The chondrocyte cell lines C28/I2, C20/A4, and T/C28a2/a4 expressed functionally active VEGFR-2. VEGF stimulation induced receptor phosphorylation, activation of the mitogen-activated protein kinases ERK 1/2, and long-lasting activation of the transcription factor AP-1 (activator protein-1). VEGF increased secreted MMP-1, MMP-3, and especially MMP-13, which could be effectively reduced by an inhibitor of VEGFR-2 kinase activity. Interestingly, VEGF diminished the expression of TIMP-1 and especially TIMP-2. Under hypoxic conditions, as occur in cartilage, the reduction in TIMP levels was even greater. Furthermore, VEGF induced IL-1beta, IL-6, TNF-alpha, and nitric oxide expression to a small extent and stimulated the proliferation of immortalized chondrocytes. These findings indicate that VEGF is an autocrine stimulator of immortalized chondrocytes that mediates mainly destructive processes in osteoarthritis.
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L7 ANSWER 12 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004302205 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15205695
TITLE: Adenovirus-mediated gene transfer of rHSG-1 inhibits proliferation of vascular smooth muscle cells from spontaneously hypertensive rats.
AUTHOR: Li Peng-fei; Guo Yan-hong; Li Qian; Yao Peng-ying; Chen Guang-hui
CORPORATE SOURCE: Peking University Institute of Cardiovascular Sciences, Beijing 100083, China.
SOURCE: Beijing da xue xue bao. Yi xue ban = Journal of Peking University. Health sciences, (2004 Jun 18) Vol. 36, No. 3, pp. 259-62.
Journal code: 101125284. ISSN: 1671-167X. L-ISSN: 1671-167X.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 24 Jun 2004
Last Updated on STN: 20 Oct 2004
Entered Medline: 19 Oct 2004

AB OBJECTIVE: To investigate the effect of rat hyperplasia suppressor gene-1(rHSG-1) on the proliferation of aortic vascular smooth muscle cells(VSMCs) from spontaneously hypertensive rats(SHR).

METHODS: VSMCs were transfected with an adenoviral vector expressing rHSG-1(Ad5rHSG-1). The effect of rHSG-1 on the proliferation of VSMCs was investigated by cell counting, MTT assay and (3)H-thymidine incorporation. We also analyzed the cell-cycle using flow cytometry and detected the expression of p27(Kip1) and p21(Cip1) by Western Blot.

RESULTS: The proliferation of VSMCs infected with Ad5rHSG-1 was inhibited a 40% reduction compared with the control group($P<0.01$). The cell cycle was arrested in G(0)/G(1) phase and the expression of p27(Kip1) and p21(Cip1) was upregulated after the VSMCs transfection with Ad5rHSG-1.

CONCLUSION: Adenovirus-mediated gene transfer of rHSG-1 inhibits the cell cycle progression and thus the proliferation of VSMCs from SHR.

L7 ANSWER 13 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004089121 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14978477
TITLE: Characterization of the roles of STAT1 and STAT3 signal transduction pathways in mammalian lens development.
AUTHOR: Ebong Samuel; Chepelinsky Ana B; Robinson Michael L; Zhao Haotian; Yu Cheng-Rong; Egwuagu Charles E
CORPORATE SOURCE: Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, MD 20892-1857, USA.
SOURCE: Molecular vision, (2004 Feb 19) Vol. 10, pp. 122-31. Electronic Publication: 2004-02-19.
Journal code: 9605351. E-ISSN: 1090-0535. L-ISSN: 1090-0535.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 24 Feb 2004
Last Updated on STN: 6 Mar 2004
Entered Medline: 5 Mar 2004

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record

AB PURPOSE: IGF-1 and PDGF are implicated in regulating lens proliferation and/or providing spatial cues that restrict lens proliferation to germinative and transition zones of the lens. However, very little is known about how IGF-1- or PDGF-induced signals are transduced and coupled to gene transcription in lens cells. Therefore, we examined whether these growth factors mediate their effects in the lens through the evolutionarily conserved JAK/STAT signal transduction pathway and if STAT signaling is essential for mammalian lens development.

METHODS: Expression of STAT1 and STAT3 was analyzed in mouse lens and lens epithelial cells by RT-PCR and western blot analysis. Activation of the STAT signaling pathway was examined by a combination of gel-shift, super-shift, and western blotting assays. Regulation of lens proliferation and gene transcription by STAT pathways was assessed by 3H-Thymidine incorporation or RT-PCR assays with lens explants treated or untreated with Genistein or the JAK2 and STAT3 inhibitor, AG-490. Mice with targeted deletion of STAT3 in the lens

were generated by Cre/lox recombination and STAT1^{-/-}, STAT3^{-/-} deficient as well as normal lenses were characterized by histology.

RESULTS: We show that PDGF and IGF1 induce proliferation in 1AMLE6 lens cells and couple their extracellular signals to gene transcription, in part through activation of STAT3 and to a lesser extent STAT1 signal transduction pathways. We further show that targeted deletion of STAT3 in E10.5 lens does not produce overt developmental lens defects. STAT1 knockout mice also exhibit a normal lens phenotype.

CONCLUSIONS: Our results showing that deletion of either STAT1 or STAT3 does not affect the normal development of the lens is surprising in view of the fact that STAT pathways are activated in developing chick or mouse lens and inappropriate activation of STAT1 pathway in the lens by ectopic lens expression of IFN γ inhibits lens differentiation and induces cataract in transgenic mice. Our data thus suggest that although STAT-signaling pathways may contribute to activation of gene transcription in the lens, it may not be essential for normal lens development or STAT proteins may be functionally redundant during lens development. However, because several growth factors and cytokines present in the lens activate STATs in mouse lens explants and 1AMLE6 lens epithelial cells, it may well be that this evolutionarily conserved signaling pathway is under stringent control in the mammalian lens. Whereas deficiency in any particular STAT pathway can be compensated for by any of the functionally redundant STAT proteins induced by a wide array of growth factors in the lens, chronic or prolonged activation of a particular STAT protein may perturb homeostatic balance in STAT-dependent growth factor signaling, culminating in pathologic lens changes.

L7 ANSWER 14 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004124369 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15015581
TITLE: The inhibitory effects of gossypol on human prostate cancer cells-PC3 are associated with transforming growth factor beta1 (TGFbeta1) signal transduction pathway.
AUTHOR: Jiang Jiahua; Sugimoto Yasuro; Liu Suling; Chang Hsiang-Lin; Park Kah-Young; Kulp Samuel K; Lin Young C
CORPORATE SOURCE: Laboratory of Reproductive and Molecular Endocrinology, College of Veterinary Medicine, The Ohio State University, 1900 Coffey Road, Columbus, OH 43210, USA.
CONTRACT NUMBER: CA66193 (United States NCI NIH HHS)
P30CA16058 (United States NCI NIH HHS)
SOURCE: Anticancer research, (2004 Jan-Feb) Vol. 24, No. 1, pp. 91-100.
Journal code: 8102988. ISSN: 0250-7005. L-ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 13 Mar 2004
Last Updated on STN: 22 May 2004
Entered Medline: 21 May 2004
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB BACKGROUND: Racemic gossypol [(+/-)-GP], a naturally occurring polyphenolic yellow pigment present in cottonseed products, inhibits in vitro proliferation of Dunning prostate cancer cells (MAT-LyLu), human prostate cancer cells derived from a bone marrow metastasis (PC3), MCF-7 and primary cultured human prostate cells. (+/-)-GP also has the ability to inhibit the metastasis of lung and lymph nodes of the androgen-independent rodent prostate cancer cell line, MAT-LyLu, after

implantation into Copenhagen rats.

MATERIALS AND METHODS: The effects of (+/-)-GP on the proliferation of human prostate cancer PC3 cells were determined by thymidine incorporation assay and doubling-time (DT) determination. The mechanisms of action of (+/-)-GP on the proliferation of PC3 cells were determined by RT-PCR analysis, ELISA assay and Western blot analysis.

RESULTS: The results show that (+/-)-GP caused reductions in DNA synthesis and prolonged the DTs in PC3 cells. RT-PCR and ELISA results show that (+/-)-GP elevate the mRNA expression and protein secretion of transforming growth factor beta1 (TGFbeta1) in PC3 cells. Consistent with these findings, (+/-)-GP has been shown to decrease the cyclin D1 mRNA expression and protein expression in PC3 cells. Furthermore, the growth inhibition of PC3 cells by conditioned media collected from the (+/-)-GP-treated-PC3 cells was completely reversed by addition of 25 microg/ml of mouse monoclonal anti-TGFbeta1, -beta2, -beta3 antibody, suggesting the involvement of TGFbeta1 in (+/-)-GP-induced growth inhibition of PC3 cells.

CONCLUSION: These results indicate that the inhibitory effects of (+/-)-GP on the proliferation of human prostate cancer PC3 cells are associated with induction of TGFbeta1, which in turn influences the expression of the cell cycle-regulatory protein, cyclin D1, in prostate cancer cells.

L7 ANSWER 15 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004383205 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15287095
TITLE: Effect of permixon on human prostate cell growth: lack of apoptotic action.
AUTHOR: Hill Brian; Kyprianou Natasha
CORPORATE SOURCE: Division of Urology, University of Maryland School of Medicine, Baltimore, MD, USA.
SOURCE: The Prostate, (2004 Sep 15) Vol. 61, No. 1, pp. 73-80.
Journal code: 8101368. ISSN: 0270-4137. L-ISSN: 0270-4137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 3 Aug 2004
Last Updated on STN: 10 Sep 2004
Entered Medline: 9 Sep 2004

AB **BACKGROUND:** Permixon, a phytotherapeutic agent derived from the saw palmetto or *Serenoa repens* plant, is a lipid/sterol extract that is believed to interfere with 5alpha-reductase activity, thus inhibiting prostate growth. In this study, we investigated the magnitude and specificity of the effect of Permixon on cell proliferation and apoptosis in human prostate cancer cells.

METHODS: The effect of Permixon was examined in androgen-independent PC-3 prostate cancer cells, androgen-sensitive LNCaP prostate cancer cells, and MCF-7 breast cancer cells in vitro. Cell growth, apoptosis induction, and cell proliferation was studied after exposure to Permixon at two concentrations (10 and 100 microg/ml). Cell proliferation and cell cycle progression were determined after 24 hr on the basis of (3)[H]-thymidine incorporation assay and flowcytometric analysis, respectively. Apoptosis

induction was evaluated in treated and untreated cultures using the Hoescht staining and caspase-3 activation.

RESULTS: Exposure of prostate and breast cancer cells to a high dose of Permixon (100 microg/ml) resulted in a significant decrease in the rate of cell growth; an effect that was not time-dependent and was not associated with cell cycle arrest. Permixon treatment (at either high or low dose) had no effect on apoptosis induction in prostate cancer cell lines ($P > 0.6$). Furthermore, in vitro Permixon was a weak inhibitor of 5alpha-reductase activity type 2 in prostatic homogenates.

CONCLUSIONS: The results indicate the ability of Permixon to affect prostate cancer cell growth without inducing apoptosis or cell cycle arrest. This effect was not prostate-specific and was only manifested at high concentrations of Permixon. Furthermore our findings indicate that Permixon is weak inhibitor of 5alpha-reductase compared to finasteride. This study challenges previous evidence on the anti-growth effect of Permixon in the prostate and its ability to inhibit 5alpha-reductase activity, while questioning apoptosis as a mechanism of action of this phytotherapeutic against prostate growth, a concept that may have therapeutic significance.

L7 ANSWER 16 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004459046 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15286442
TITLE: Intratracheal instillation of cytoplasmic granules from Phleum pratense pollen induces IgE- and cell-mediated responses in the Brown Norway rat.
AUTHOR: Motta A C; Dormans J A; Peltre G; Lacroix G; Bois F Y; Steerenberg P A
CORPORATE SOURCE: National Institute of Public Health and the Environment, NA-3720 BA Bilthoven, The Netherlands.
Alexandre.Motta@rivm.nl
SOURCE: International archives of allergy and immunology, (2004 Sep) Vol. 135, No. 1, pp. 24-9. Electronic Publication: 2004-07-29.
Journal code: 9211652. ISSN: 1018-2438. L-ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 16 Sep 2004
Last Updated on STN: 15 Oct 2004
Entered Medline: 14 Oct 2004
AB BACKGROUND: Release of cytoplasmic granules from grass pollen upon contact with water is thought to be an important source of airborne allergens.

OBJECTIVES: To investigate the humoral and cellular responses to intratracheal instillation of Phleum pratense (timothy grass) pollen cytoplasmic granules (PCG) in the Brown Norway rat.

METHODS: PCG were purified from timothy grass pollen by filtration through 5-microm-mesh filters. Rats were sensitized (day 0) and challenged (day 21) intratracheally with purified PCG suspended in saline (6×10^6 PCG/rat). Rats were then challenged 4 weeks later (1.5×10^6 PCG/rat). Blood samples, bronchial lymph nodes and lungs were collected from the rats 4 days after the second challenge. PCG-specific IgE and IgG1 levels and specificity were determined by ELISA and Western blotting. Pollen, pollen extract and PCG-induced proliferation

of lymph node cells were monitored by [(3)H]-thymidine incorporation in a lymph node assay. Histopathological examination was carried out on the lungs.

RESULTS: Specific IgE and IgG1 were present in the sera. Cultured lymph node cells proliferated in the presence of pollen, pollen extract and PCG. Western blots showed that all major pollen allergens are recognized by IgE and IgG1 from PCG-treated rats. Histopathological examination revealed features of a mild allergic reaction.

CONCLUSIONS: In our rat model of allergy, purified timothy grass PCG instillation induced specific antibodies and lymph node cell responses, comparable to those obtained with intact pollen.

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L7 ANSWER 17 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003536555 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12920044
TITLE: Heparin inhibition of endothelial cell proliferation and organization is dependent on molecular weight.
AUTHOR: Khorana Alok A; Sahni Abha; Altland Owen D; Francis Charles W
CORPORATE SOURCE: James P. Wilmot Cancer Center and Hematology/Oncology Unit, Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY14642, USA.
CONTRACT NUMBER: HL-30616 (United States NHLBI NIH HHS)
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (2003 Nov 1) Vol. 23, No. 11, pp. 2110-5.
Electronic Publication: 2003-08-14.
Journal code: 9505803. E-ISSN: 1524-4636. L-ISSN: 1079-5642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 18 Nov 2003
Last Updated on STN: 7 Apr 2004
Entered Medline: 6 Apr 2004
OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB OBJECTIVE: Studies have shown improved survival in cancer patients treated with low molecular weight heparins (LMWHs). Tumors depend on an expanding vasculature, and heparins may affect vessel growth and function. We investigated the effect of heparins differing in Mr on selected endothelial cell properties.

METHODS AND RESULTS: Human umbilical vein endothelial cells were cultured with fibroblast growth factor-2 and heparins differing in Mr. Cell proliferation was assessed by [3H]thymidine incorporation, and vascular organization was assessed by in vitro assays. Maximum inhibition of 94+/-2% was observed with 6-kDa LMWH, greater than the inhibition seen with unfractionated heparin (58+/-8%) or 3-kDa LMWH (60+/-9%, P=0.02 for both). No inhibition of proliferation was observed with heparin tetrasaccharide, octasaccharide, or pentasaccharide (fondaparinux). Three- and 6-kDa fractions decreased endothelial tube formation in Matrigel to 58+/-15% and 67+/-9% (P<0.05), respectively, of that with fibroblast growth factor-2, whereas no inhibition was observed with unfractionated heparin, tetrasaccharide, pentasaccharide, or octasaccharide. LMWH (6 kDa) also inhibited vessel formation in a placental explant.

CONCLUSIONS: Heparin inhibition of endothelial cell proliferation and organization requires a chain length of >8 saccharide units, with maximal inhibition at Mr of 6 kDa. This Mr dependence differs from that required for anticoagulant activity.

L7 ANSWER 18 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003555356 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14616867
TITLE: Ebastine inhibits T cell migration, production of Th2-type cytokines and proinflammatory cytokines.
AUTHOR: Nori M; Iwata S; Munakata Y; Kobayashi H; Kobayashi S; Umezawa Y; Hosono O; Kawasaki H; Dang N H; Tanaka H; Shiohara T; Morimoto C
CORPORATE SOURCE: Division of Clinical Immunology, Advanced Clinical Research Center, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo, Japan.
SOURCE: Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology, (2003 Nov) Vol. 33, No. 11, pp. 1544-54.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 26 Nov 2003
Last Updated on STN: 3 Feb 2004
Entered Medline: 2 Feb 2004
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB BACKGROUND: Cytokine imbalance and cellular migration to inflammatory sites are critical components of allergic diseases. Redirecting cytokine imbalance and inhibiting cell migration therefore represent important therapeutic strategies for the treatment of these disorders.

OBJECTIVES: To study the in vitro effect of ebastine, a novel non-sedating H1 receptor antagonist, on cytokine secretion and migration of activated T cells, as well as production of pro-inflammatory cytokines by macrophages.

METHODS: Peripheral T cells obtained from healthy volunteers were cultured in wells coated with the combination of anti-CD3 monoclonal antibody (mAb) and anti-CD26 mAb, anti-CD3 mAb and anti-CD28 mAb, or anti-CD3 mAb with PMA, in the presence or absence of ebastine. T cell proliferation and the production of cytokines were measured by [3H]thymidine incorporation assay and ELISA, respectively. In addition, transendothelial migration of T cells and production of pro-inflammatory cytokines by macrophages were examined.

RESULTS: Ebastine inhibited T cell proliferation and the production of IL-4, IL-5, IL-6, and TNF-alpha by T cells under each co-stimulatory condition tested, whereas it exhibited no effect on the production of IL-2 or IFN-gamma. In addition, T cell migration and the production of such pro-inflammatory cytokines as TNF-alpha and IL-6 by macrophages were inhibited by ebastine.

CONCLUSIONS: These results indicate that ebastine has a specific inhibitory effect on Th2-type cytokine production. Moreover, ebastine inhibited T cell migration and pro-inflammatory cytokine production by T cells and macrophages, suggesting that ebastine might be useful for the treatment of T cell-mediated allergic inflammatory disorders, including

asthma, atopic dermatitis, and Th2-type autoimmune diseases.

L7 ANSWER 19 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003465871 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14527367
TITLE: Inhibition of lovastatin on proliferation and expression of proinflammatory cytokines in cultured human glomerular mesangial cells.
AUTHOR: Li Hang; Li Xuewang; Duan Lin; Li Chenhong
CORPORATE SOURCE: Department of Nephrology, Peking Union Medical College Hospital, Beijing 100730, China.
SOURCE: Chinese medical journal, (2003 Sep) Vol. 116, No. 9, pp. 1366-9.
Journal code: 7513795. ISSN: 0366-6999. L-ISSN: 0366-6999.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 8 Oct 2003
Last Updated on STN: 5 Feb 2004
Entered Medline: 4 Feb 2004
AB OBJECTIVE: To study the effects and mechanism of lovastatin on cell proliferation and expression of proinflammatory cytokines in cultured human glomerular mesangial cells.

METHODS: The influence of lovastatin on HMC proliferation was evaluated with 3H-thymidine incorporation. mRNA expression of proinflammatory cytokines (IL-1 beta, IL-6, TNF-alpha, and MCP-1) and activation of NF-kappa B of HMC were measured using Reverse transcription-polymerase chain reaction (RT-PCR) and electrophoretic mobility shift assay (EMSA) respectively.

RESULTS: Lovastatin was found to have inhibitory effects on human mesangial cell (HMC) proliferation and lipopolysaccharide (LPS)-mediated human mesangial cell HMC mRNA expression of proinflammatory cytokines via activation of NF-kappa B. The effect of lovastatin on HMC could be prevented when the mevalonate and farnesol were added to the culture.

CONCLUSION: Lovastatin may decrease HMC proliferation and production of proinflammatory cytokines through the inhibition of NF-kappa B activation. This provided experimental evidence for further evaluation of the renal protective effect of HRI, suggesting that it may be a potent agent for prevention of progressive renal diseases aside from its lipid-lowering effect.

L7 ANSWER 20 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003508114 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14584865
TITLE: Platelet-derived growth factor-BB stimulated cell migration mediated through p38 signal transduction pathway in periodontal cells.
AUTHOR: Ray Angel K; Jones Anne C; Carnes David L; Cochran David L; Mellonig James T; Oates Thomas W Jr
CORPORATE SOURCE: Department of Pathology, University of Texas Health Science Center, San Antonio, TX 78229-3900, USA.
SOURCE: Journal of periodontology, (2003 Sep) Vol. 74, No. 9, pp. 1320-8.
Journal code: 8000345. ISSN: 0022-3492. L-ISSN: 0022-3492.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 31 Oct 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 16 Dec 2003

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: Intracellular signaling pathways mediate specific responses to growth factors. The manipulation of these pathways ultimately may be used to control the clinical outcomes of periodontal regenerative therapy. The purpose of this study was to examine the role of the p38 signal transduction pathway in the responses of periodontal cells to platelet-derived growth factor-BB (PDGF).

METHODS: Primary cultures of human periodontal ligament cells (PDLs) and gingival fibroblasts (GFs) were used for all experiments. Cell numbers, 3H-thymidine incorporation, and Boyden chamber assays were used to characterize the effects of SB 203580 (SB), a specific inhibitor of the p38 signaling pathway, on cell proliferation and migration. An in vitro wound model also was used to assess the effects of SB. For the in vitro wound assay, triplicate wells were incubated for 1, 3, 5, and 7 days using 0.1% fetal bovine serum (FBS), 10% FBS +/- 10 microM SB, or 20 ng/ml PDGF +/- 10 microM SB. Digital histomorphometric analysis assessed cellular fill within the wound area.

RESULTS: SB specifically inhibited PDGF-induced migration in the Boyden chamber assays without affecting cell proliferation. The wound model data showed similar levels of wound fill for PDLs and GFs in 10% FBS. Relative to 10% FBS, PDLs stimulated with PDGF showed significantly ($P < 0.01$, analysis of variance) greater wound fill (74%) than GFs (12%). SB inhibited the PDGF-induced wound fill of PDLs and GFs by 64% and 57%, respectively. This inhibition was significant ($P < 0.01$, ANOVA) only for PDLs. The addition of SB to 10% FBS did not significantly affect the wound fill response of either cell type compared to 10% FBS alone.

CONCLUSIONS: These results demonstrate that periodontal cells possess distinct responses to PDGF that may be altered at the signal transduction level. The manipulation of these responses through the use of inhibitors to specific signaling pathways may enhance our control of periodontal regeneration in the future.

L7 ANSWER 21 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003273573 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12800222
TITLE: Development of an oral DNA vaccine against MG7-Ag of gastric cancer using attenuated salmonella typhimurium as carrier.
AUTHOR: Guo Chang-Cun; Ding Jie; Pan Bo-Rong; Yu Zhao-Cai; Han Quan-Li; Meng Fan-Ping; Liu Na; Fan Dai-Ming
CORPORATE SOURCE: Institute of Digestive Disease, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China.
SOURCE: World journal of gastroenterology : WJG, (2003 Jun) Vol. 9, No. 6, pp. 1191-5.
Journal code: 100883448. ISSN: 1007-9327. L-ISSN: 1007-9327.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309

ENTRY DATE: Entered STN: 12 Jun 2003
Last Updated on STN: 13 Sep 2003
Entered Medline: 12 Sep 2003
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB AIM: To develop an oral DNA vaccine against gastric cancer and evaluate its efficacy in mice.

METHODS: The genes of the MG7-Ag mimotope and a universal Th epitope (Pan-DR epitope, PADRE) were included in the PCR primers. By PCR, the fusion gene of the two epitopes was amplified. The fusion gene was confirmed by sequencing and was then cloned into pcDNA3.1(+) plasmid. The pcDNA3.1 (+)-MG7/PADRE was used to transfect an attenuated *Salmonella typhimurium*. C57BL/6 mice were orally immunized with 1×10^8 cfu *Salmonella* transfectants. *Salmonella* harboring the empty pcDNA3.1(+) plasmid and phosphate buffer saline (PBS) were used as negative controls. At the 6th week, serum titer of MG7-Ag specific antibody was detected by ELISA. At the 8th week cellular immunity was detected by an unprimed proliferation test of the spleenocytes by using a ((3)H)-thymidine incorporation assay. Ehrlich ascites carcinoma cells expressing MG7-Ag were used as a model in tumor challenge assay to evaluate the protective effect of the vaccine.

RESULTS: Serum titer of antibody against MG7-Ag was significantly higher in mice immunized with the vaccine than that in control groups (0.841 vs 0.347, $P < 0.01$; 0.841 vs 0.298, $P < 0.01$), while in vitro unprimed proliferation assay of the spleenocytes showed no statistical difference between those three groups. Two weeks after tumor challenge, 2 in 7 immunized mice were tumor free, while all the mice in the control groups showed tumor formation.

CONCLUSION: Oral DNA vaccine against the MG7-Ag mimotope of gastric cancer is immunogenic. It can induce significant humoral immunity against tumor in mice, and the vaccine has partially protective effects.

L7 ANSWER 22 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003612095 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14674894
TITLE: Methylisothiazolinones elicit increased production of both T helper (Th)1- and Th2-like cytokines by peripheral blood mononuclear cells from contact allergic individuals.
AUTHOR: Masjedi K; Ahlborg N; Gruvberger B; Bruze M; Karlberg A-T
CORPORATE SOURCE: Department of Medicine, Unit of Clinical Allergy Research, Karolinska Institutet and Hospital, Stockholm, Sweden.
SOURCE: The British journal of dermatology, (2003 Dec)
Vol. 149, No. 6, pp. 1172-82.
Journal code: 0004041. ISSN: 0007-0963. L-ISSN: 0007-0963.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 30 Dec 2003
Last Updated on STN: 12 Mar 2004
Entered Medline: 11 Mar 2004

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: Delayed-type hypersensitivity reactions to nickel (Ni2+) in humans are associated with increased production of both T helper (Th) 1- and Th2-like cytokines. Cytokine responses to the major group of contact allergens, i.e. organic compounds, have been less extensively studied. We have investigated here the cytokine production induced by a mixture of methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI), the

active ingredients in common preservatives that are capable of eliciting allergic contact dermatitis.

OBJECTIVE: To characterize the immune response induced by MCI/MI in terms of the production of Th1- and Th2-like cytokines in peripheral blood mononuclear cells (PBMC) from allergic and non-allergic subjects.

METHODS: Ten subjects with a history of contact allergy to MCI/MI and nine age-matched non-allergic volunteers participated. Their actual status was confirmed by patch testing. PBMC were cultured in the presence or absence of MCI/MI; cell proliferation was measured employing [3H]thymidine incorporation; and the number of cytokine-producing cells was determined using the enzyme-linked immunospot (ELISpot) assay and the levels of soluble cytokines in culture media by the enzyme-linked immunosorbent assay (ELISA).

RESULTS: The proliferative response of PBMC to MCI/MI was significantly greater in the case of the allergic group than for the non-allergic group, as was the production of interleukin (IL)-2 and IL-13 (as determined by ELISpot and/or ELISA). PBMC from three of the allergic individuals with increased production of IL-2 and IL-13 responded to MCI/MI with elevated numbers of cells producing IL-4 and IL-5. The increases in the production of IL-2, IL-4, IL-5 and IL-13 were positively correlated.

CONCLUSION: MCI/MI elicited concomitant production of both Th1- and Th2-like cytokines by PBMC from subjects with contact allergy to these substances. This finding indicates that the organic compounds MCI/MI elicit a mixed Th1- and Th2-type of response, similar to that elicited by the metal ion Ni2+ in Ni2+-sensitized individuals.

L7 ANSWER 23 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003340014 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12631069
TITLE: Monocyte adhesion to mesangial matrix modulates cytokine and metalloproteinase production.
AUTHOR: Chana Ravinder S; Martin John; Rahman Enam U; Wheeler David C
CORPORATE SOURCE: Department of Nephrology, University Hospital Birmingham NHS Trust, London, United Kingdom.
SOURCE: Kidney international, (2003 Mar) Vol. 63, No. 3, pp. 889-98.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal code: 0323470. ISSN: 0085-2538. L-ISSN: 0085-2538. Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: (RESEARCH SUPPORT, NON-U.S. GOV'T)
ENTRY MONTH: English
ENTRY DATE: Priority Journals
OS.CITING REF COUNT: 1 Entered STN: 23 Jul 2003
AB BACKGROUND: Monocytes migrate into the glomerular mesangium during acute inflammatory renal disease, differentiate into macrophages, and may play a key role in the development and progression of glomerular scarring. Treatment strategies that inhibit monocyte infiltration ameliorate glomerular injury in animal models. Mesangial matrix contains several potential monocyte-binding domains that may contribute to monocyte entrapment and modulate cell activation.
METHODS: Adhesion of peripheral blood-derived monocytes to
Last Updated on STN: 2 Mar 2004
Entered Medline: 26 Feb 2004
There are 1 MEDLINE records that cite this record

matrix synthesized by human mesangial cells and to individual matrix proteins was assessed by colorimetry of nuclear staining with crystal violet. Monoclonal antibodies were used to identify the cell-surface integrins and matrix ligands involved. Monocyte proliferation was assessed by 3H-thymidine incorporation and cytokine production using enzyme-linked immunosorbent assay (ELISA). Secretion of metalloproteinases and their inhibitors was determined by zymography and ELISA, respectively.

RESULTS: Monocytes bound to matrix synthesized by mesangial cells. Prestimulation of mesangial cells with tumor necrosis factor-alpha (TNF-alpha) and transforming growth factor-beta (TGF-beta) enhanced matrix fibronectin content (P < 0.001) and monocyte binding (P < 0.001). Blocking antibodies to fibronectin, as well as to the integrins very late antigen-4 (VLA-4) and VLA-5, reduced monocyte adhesion to mesangial matrix by approximately 50%. Incubation of monocytes with matrix, fibronectin, laminin and collagen IV enhanced production of interleukin-1beta (IL-1beta), interleukin-6 (IL-6), TNF-alpha and metalloproteinase-9 (MMP-9) when compared to cells incubated in plastic wells. However, there was no apparent difference in proliferation rate and no change in production of metalloproteinase inhibitors.

CONCLUSION: Monocyte activation within the glomerulus may be mediated by binding to mesangial matrix components, particularly fibronectin. Matrix-mediated activation enhances production of inflammatory cytokines and matrix-degrading enzymes.

L7 ANSWER 24 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003481470 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14560235
TITLE: Overexpression of mutated IkappaBalpha inhibits vascular smooth muscle cell proliferation and intimal hyperplasia formation.
AUTHOR: Zuckerbraun Brian S; McCloskey Carol A; Mahidhara Raja S; Kim Peter K M; Taylor Bradley S; Tzeng Edith
CORPORATE SOURCE: Department of Surgery, University of Pittsburgh School of Medicine, 3459 Fifth Avenue, Pittsburgh, PA 15213, USA. zuckerbraun@msx.upmc.edu
CONTRACT NUMBER: R01 HL 57854-05 (United States NHLBI NIH HHS)
SOURCE: Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Association for Cardiovascular Surgery, North American Chapter, (2003 Oct) Vol. 38, No. 4, pp. 812-9. Journal code: 8407742. ISSN: 0741-5214. L-ISSN: 0741-5214. United States
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 16 Oct 2003
Last Updated on STN: 31 Oct 2003
Entered Medline: 30 Oct 2003
OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
AB PURPOSE: Vascular injury and inflammation are associated with elaboration of a number of cytokines that signal through multiple pathways to act as smooth muscle cell (SMC) mitogens. Activation of the nuclear factor-kappa B (NF-kappaB) transcription factor is essential for SMC proliferation in vitro and is activated by vascular injury in vivo. Activation of NF-kappaB is controlled by several upstream regulators, including the inhibitors of kappa B (IkappaB). These proteins bind to and keep

NF-kappaB inactivated. The purpose of this study was to determine whether adenoviral gene transfer of a mutated IkappaBalpha super-repressor (AdIkappaBalphaSR) could inhibit development of intimal hyperplasia in vivo and to investigate how over-expression of this construct influences in vitro SMC proliferation and cell cycle regulatory proteins.

METHODS: A rat carotid injury model was used to study prevention of intimal hyperplasia. Arteries were assayed 14 days after injury and infection with AdIkappaBalphaSR or adenoviral beta-galactosidase (AdLacZ). Untreated SMC or SMC infected with AdLacZ or AdIkappaBalphaSR were stimulated with 10% fetal bovine serum, interleukin-1beta, or tumor necrosis factor-alpha. Electrophoretic mobility shift assays were used to assay for NF-kappaB activation. Protein levels of IkappaBalpha and cyclin-dependent kinase inhibitors p21(Cip1/Waf1) and p27(Kip1) were determined with Western blot analysis. Proliferation was measured with (3)H-thymidine incorporation assays.

RESULTS: AdIkappaBalphaSR inhibited the development of intimal hyperplasia by 49% (P < .05). Infection with AdIkappaBalphaSR significantly suppressed in vitro SMC proliferation when stimulated with serum, interleukin 1, or tumor necrosis factor alpha, and did not result in cell death. Inhibition of proliferation was associated with increased p21(Cip1/Waf1) and p27(Kip1) protein levels.

CONCLUSIONS: Gene transfer of IkappaBalpha super-repressor inhibited development of intimal hyperplasia in vivo and SMC proliferation in vitro. The antiproliferative activity may be related to cell cycle arrest through upregulation of the cyclin-dependent kinase inhibitors p21 and p27. Overexpression of IkappaBalpha may be a future therapeutic option in treatment of vascular diseases.

L7 ANSWER 25 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2004031187 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14730894
TITLE: Culture of neural stem cells from cerebral cortex of rat embryo and effects of drugs on the proliferation ability of stem cells.
AUTHOR: Shen Li-hong; Zhang Jun-tian
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing 100050, China.
SOURCE: Yao xue xue bao = Acta pharmaceutica Sinica, (2003 Oct) Vol. 38, No. 10, pp. 735-8.
Journal code: 21710340R. ISSN: 0513-4870. L-ISSN: 0513-4870.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 21 Jan 2004
Last Updated on STN: 18 Aug 2004
Entered Medline: 17 Aug 2004
AB AIM: To establish culture procedures of neural stem cells from embryonic rat brain, determine their stem-cell characteristics and observe the effects of several compounds on their proliferation ability.

METHODS: Firstly, a stem cell culture system was set up from embryonic rat cortex. The cells were identified as neural stem cells through immunocytochemistry, in which antibodies to neural stem cell

specific protein and markers of mature neural cells were used. Then, by using MTT assay, the survival rate of neurospheres incubated with various concentrations of ginsenoside Rg1, (-)-clausenamide and salvianolic acid A were observed. Furthermore, the effect of these drugs was measured with ³[H] thymidine incorporation assay.

RESULTS: In this study, a culture model of neural stem cell was successfully set up. In this model, primary cells from E16-18 rat cortex were dissected out, and cultured as floating neurospheres. The results of immunocytochemistry showed that nestin was expressed by the majority of cells within the sphere. After growing for 8 days in differentiation medium, cells from a single neurosphere were shown to differentiate into 3 main kinds of neural cells: neurons, astrocytes and oligodendrocytes. MTT assay revealed that the three drugs all enhanced the survival rate of neural stem cells, but ³[H] thymidine incorporation assay suggested that only Rg1 significantly accelerated the proliferation rate.

CONCLUSION: One culture model of neural stem cell was set up successfully. Meanwhile, several drugs were found to increase the proliferation and/or survival rate of neural stem cells. It has been demonstrated that neural stem cells exist in adult mammalian brains. So, these drugs may become promising candidates for the therapy of neurodegenerative diseases; such as Alzheimer's disease and Parkinson's disease.

L7 ANSWER 26 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003282961 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12743698
TITLE: Kallikrein-binding protein inhibits retinal neovascularization and decreases vascular leakage.
AUTHOR: Gao G; Shao C; Zhang S X; Dudley A; Fant J; Ma J-X
CORPORATE SOURCE: Department of Ophthalmology, Medical University of South Carolina, 167 Ashley Ave., Charleston, SC 29425, USA.
CONTRACT NUMBER: EY 12600 (United States NEI NIH HHS)
SOURCE: Diabetologia, (2003 May) Vol. 46, No. 5, pp. 689-98. Electronic Publication: 2003-05-13. Journal code: 0006777. ISSN: 0012-186X. L-ISSN: 0012-186X.
PUB. COUNTRY: Germany; Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 18 Jun 2003
Last Updated on STN: 31 Mar 2004
Entered Medline: 30 Mar 2004
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB AIMS/HYPOTHESIS: Kallikrein-binding protein (KBP) is a serine proteinase inhibitor (serpin). It specifically binds to tissue kallikrein and inhibits kallikrein activity. Our study was designed to test its effects on retinal neovascularization and vascular permeability.

METHODS: Endothelial cell proliferation was determined by [³H] thymidine incorporation assay and apoptosis quantified by Annexin V staining and flow cytometry. Effect on retinal neovascularization was determined by fluorescein angiography and count of pre-retinal vascular cells in an oxygen-induced retinopathy (OIR) model. Vascular permeability was assayed by the Evans blue method. Vascular endothelial growth factor (VEGF) was measured by Western blot analysis and ELISA.

RESULTS: Kallikrein-binding protein specifically inhibited proliferation and induced apoptosis in retinal capillary endothelial cells. Intravitreal injection of KBP inhibited retinal neovascularization in an OIR model. Moreover, KBP decreased vascular leakage in the retina, iris and choroid in rats with OIR. Blockade of kinin receptors by specific antagonists showed significantly weaker inhibition of endothelial cells, when compared to that of KBP, suggesting that the anti-angiogenic activity of KBP is not through inhibiting kallikrein activity or kinin production. KBP competed with (125)I-VEGF for binding to endothelial cells and down-regulated VEGF production in endothelial cells and in the retina of the OIR rat model.

CONCLUSION/INTERPRETATION: Kallikrein-binding protein is a multi-functional serpin, and its vascular activities are independent of its interactions with the kallikrein-kinin system. Inhibition of VEGF binding to its receptors and down-regulation of VEGF expression could represent a mechanism for the vascular activities of KBP.

L7 ANSWER 27 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2003198163 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12679907
 TITLE: Effects of astragali radix on the growth of different cancer cell lines.
 AUTHOR: Lin Jiang; Dong Hui-Fang; Oppenheim J J; Howard O M
 CORPORATE SOURCE: Department of Gastroenterology, Shuguang Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 200021, China. lin_jiang@hotmail.com
 SOURCE: World journal of gastroenterology : WJG, (2003 Apr) Vol. 9, No. 4, pp. 670-3. Journal code: 100883448. ISSN: 1007-9327. L-ISSN: 1007-9327.
 PUB. COUNTRY: China
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200307
 ENTRY DATE: Entered STN: 30 Apr 2003
 Last Updated on STN: 30 Jul 2003
 Entered Medline: 29 Jul 2003
 OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
 AB AIM: To investigate the inhibitory effect of a Chinese herb medicine Astragali radix (AR) on growth of different cancer cell line.

METHODS: To observe the in vitro effects of AR on tumor cell proliferation by trypan blue exclusion, MTS method and tritium thymidine incorporation assay. Apoptosis was detected by DNA ladder method.

RESULTS: The inhibition rates of AR on the cell respiration of AGS, KATOIII, HT29, MDA231, MEL7 and MEL14 were 68.25 %, 62.36 %, 22.8 %, 27.69 %, 2.85 % and 5.14 % respectively at the concentration of 100 ug/ml; it inhibited AGS DNA synthesis by 87.33 % at the concentration of 50 ug/ml. The inhibitory effect on AGS was time-and dose-dependent. AR did not induce apoptosis in AGS cells.

CONCLUSION: AR specifically inhibits gastric cancer cells growth in vitro and the mechanism is mainly cytostatic but not cytotoxic or inducing apoptosis.

L7 ANSWER 28 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2003151922 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12667220
 TITLE: Divergence of contact hypersensitivity in vivo compared with hapten-specific lymphocyte proliferation and interferon-gamma production in vitro following ultraviolet B irradiation: the possibility that UVB does not affect the sensitizing phase of contact hypersensitivity.
 AUTHOR: Suzuki Kayano; Kanamori Sachio; Takada Kaori; Kawana Seiji
 CORPORATE SOURCE: Department of Dermatology, Nippon Medical School, Tokyo, Japan. kayano@nms.ac.jp
 SOURCE: Immunology, (2003 Apr) Vol. 108, No. 4, pp. 570-8.
 Journal code: 0374672. ISSN: 0019-2805. L-ISSN: 0019-2805.
 Report No.: NLM-PMC1782921.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200306
 ENTRY DATE: Entered STN: 2 Apr 2003
 Last Updated on STN: 8 Jun 2003
 Entered Medline: 6 Jun 2003

MEDLINE REFERENCE COUNT: 16 There are 16 cited references available in MEDLINE for this document.

AB A hapten-specific lymphocyte proliferation assay, which measures the in vitro stimulation of DNA synthesis (as assessed by [3H]thymidine incorporation), was used to determine systemic immunization induced by an epicutaneously applied hapten in addition to the more commonly used method which measures ear (or footpad) swelling. 2,4-Dinitrofluorobenzene (DNFB) was painted on the shaved backs of C57BL/6 mice for two consecutive days after ultraviolet B (UVB) irradiation (at 1000 J/m²), and DNFB-sensitized lymph node cells (LNC) were obtained from the regional lymph nodes 4 days later. Although the ear swelling response (ESR) was suppressed by UVB radiation, as previously reported, analysis of LNC culture supernatants showed that the production of interferon-gamma, a Tc1-type cytokine, was not inhibited by the UVB irradiation. In addition, contact dermatitis was induced (at levels similar to those of non-irradiated mice) by painting DNFB on the abdomen as a secondary response. We then examined the effect of UVB exposure alone on the ESR by injecting a mast cell degranulator, compound 48/80, 7 days after irradiation. Both the ESR and the percentage of degranulated mast cells were significantly reduced in UVB-irradiated mice. These results demonstrate that UVB irradiation does not affect the sensitizing phase of contact hypersensitivity, but modulates the elicitation phase and reduces the ESR primarily by suppressing the degranulation of mast cells. Therefore, suppression of the ESR alone cannot always be considered as hapten-specific immunotolerance.

L7 ANSWER 29 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2003523453 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14594509
 TITLE: Functional evaluation of proliferative T cell responses in patients with severe T lymphopenia: characterization of optimal culture conditions and standardized activation signals for a simple whole blood assay.
 AUTHOR: Wendelbo Oystein; Bruserud Oystein
 CORPORATE SOURCE: Division for Hematology, Department of Medicine, Haukeland University Hospital, Bergen, Norway. wend@haukeland.no
 SOURCE: Journal of hematology
 & stem cell research, (2003 Oct) Vol. 12, No. 5, pp. 525-35.
 Journal code: 100892915. ISSN: 1525-8165. L-ISSN: 1525-8165.

PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 7 Nov 2003
Last Updated on STN: 10 Jun 2004
Entered Medline: 9 Jun 2004

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB In this methodological study, we describe an assay for analysis of proliferative T cell responses in patients with severe leukopenia. Severe treatment-induced cytopenia is observed in patients with malignant disorders who receive conventional intensive chemotherapy or autologous stem cell transplantation. The quantitative T cell defect can then be characterized by flow cytometric analysis of membrane molecule expression, whereas the functional status of the remaining T cell population is more difficult to evaluate. In the present study, we describe a standardized whole blood assay that requires small sample volumes and can be used for repeated analysis even in severely ill patients. The assay is based on the following strategy: (i) blood samples are diluted with the serum-free medium X-vivo 10, (ii) T cells are activated either with monoclonal immunoglobulin E (IgE) anti-CD3 or anti-CD3 plus anti-CD28; (iii) T cell proliferation is assayed by [(3)H]thymidine incorporation after 4 days of in vitro culture. These proliferative responses are not affected by the plasma levels of interleukin-2 (IL-2), sIL-2-R alpha, IL-7 and IL-15, and the kinetics of the response are not altered by the presence of exogenous cytokines. Detectable proliferation is observed for most patients with treatment-induced cytopenia. We conclude that the assay can be used for functional characterization of remaining T lymphocytes in patients with severe T lymphopenia.

L7 ANSWER 30 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003376511 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12910695
TITLE: The effects of selective cyclooxygenase-2 inhibitors on the growth of gastric adenocarcinoma.
AUTHOR: Liu Chunlun; Tang Chengwei; Wan Xuehong; Wang Chunhui; Zhou Xuchun
CORPORATE SOURCE: Department of Gastroenterology, First Hospital of Chongqing Medical University, Chongqing 400016, China.
SOURCE: Sichuan da xue xue bao. Yi xue ban = Journal of Sichuan University. Medical science edition, (2003 Jul)
Vol. 34, No. 3, pp. 480-3.
Journal code: 101162609. ISSN: 1672-173X. L-ISSN: 1672-173X.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 23 Jul 2004
Entered Medline: 22 Jul 2004

AB OBJECTIVE: This study was aimed to compare the effects of three kinds of selective cyclooxygenase-2 inhibitors (meloxicam, celecoxib, rofecoxib) on the growth of gastric adenocarcinoma SGC7901 cell line, and to observe the effect of rofecoxib, on transplanted gastric cancer of nude mice in vivo.

METHODS: The proliferation and apoptosis of SGC7901 cells were measured by ³H-thymidine incorporation into DNA and the TdT-mediated dUTP nick end-labeling assay (TUNEL) separately. The expression of PCNA and COX-2 of gastric adenocarcinoma cells were detected by immunocytochemistry. Human gastric adenocarcinoma SGC7901 cells were implanted orthotopically in the stomach of nude mice. Rofecoxib (30 mg.kg-1.d-1) was administrated i.g. for eight weeks.

RESULTS: All the drugs potentially decreased ³H-thymidine incorporation into SGC7901 cells. The inhibition effects showed a dose-dependence manner. The median-response concentration was: 1.18 x 10⁻⁷ mol/L (meloxicam), 1.68 x 10⁻⁸ mol/L (celecoxib), 4.39 x 10⁻⁹ mol/L (rofecoxib). After treatment with meloxicam, celecoxib, rofecoxib (1 x 10⁻⁵ mol/L) for 24 hours, the apoptosis indices of SGC7901 cells were: 19.8% +/- 1.8%, 24.6% +/- 1.2% and 31.2% +/- 2.2%, respectively. The higher selective inhibition on COX-2, the higher apoptosis index (P < 0.01). Rofecoxib down-regulated the expression of COX-2 and PCNA of SGC7901 cell, both in vitro and in vivo. The inhibition rate for xenografts in situ in nude mice treated with rofecoxib was 93.9%.

CONCLUSION: The higher selective inhibition on COX-2, the stronger inhibition on gastric adenocarcinoma cells. Rofecoxib may be one of the important medicines in the treatment of gastric adenocarcinoma.

L7 ANSWER 31 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003573715 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14646595
TITLE: High efficiency transduction of human VEGF165 into human skeletal myoblasts: in vitro studies.
AUTHOR: Ye Lei; Haider Husnain Kh; Jiang Shujia; Ge Ruowen; Law Peter K; Sim Eugene K W
CORPORATE SOURCE: Department of Cardiothoracic and Vascular Surgery, National University of Singapore, Singapore-117597.
SOURCE: Experimental & molecular medicine, (2003 Oct 31)
Vol. 35, No. 5, pp. 412-20.
Journal code: 9607880. ISSN: 1226-3613. L-ISSN: 1226-3613.
PUB. COUNTRY: Korea (South)
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 27 Aug 2004
Entered Medline: 26 Aug 2004
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB We report the transduction of human VEGF165 gene into human myoblast and characterization of the transduced myoblasts for transduction and expression efficiency. Human myoblasts were assessed by immunostaining for desmin expression. A replication incompetent adenoviral vector carrying human VEGF165 was constructed and used for transduction of myoblasts. Immunostaining of transduced myoblasts was used to determine transduction efficiency. Expression efficiency was confirmed by immunoblotting, ELISA and reverse transcription (RT)-PCR analysis using human VEGF165 specific primers (5'-3' = 5'ATGAACCTTCTGCTGTCTTGGGTG and 3'-5' = ACACCGCCTCGGCTTGTCACA3'. Biological activity of the secreted VEGF165 was determined by human umbilical vein endothelial cell proliferation and [³H] thymidine incorporation assays. Human myoblast preparation was >95% pure with 99% viability after transduction. Immunostaining showed >95% VEGF(165) positive myoblasts. Western blotting and ELISA revealed high VEGF165

expression in the transduced myoblasts. Maximum transduction efficiency was achieved by 8 h exposure of myoblasts to virus at 1:1,000 ratio on three consecutive days. Concentration of VEGF165 released in the culture medium peaked (37 +/- 3 ng/ml) at 8 days post-transduction. Cell proliferation assay on human umbilical vein endothelial cells using supernatant from VEGF165 transduced myoblasts revealed extensive proliferation of cells which was suppressed in the presence of anti-human VEGF165 antibody in culture medium and was further confirmed by thymidine incorporation assay. The untransduced myoblasts secreted VEGF165 in vitro (300 +/- 50 pg/ml) that is enhanced many folds (37 +/- 3 ng/ml) in VEGF165 transduced myoblast as determined by ELISA. These studies suggest that human myoblast are potential carriers of human VEGF165 to achieve concurrent angiogenesis for cardiac repair.

L7 ANSWER 32 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2003366805 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12899770
 TITLE: The inhibitory mechanism of nitric-oxide synthase gene transfection on hypoxia-induced proliferation of rat pulmonary arterial smooth muscle cells.
 AUTHOR: Zeng Qiong; Ran Pi-xin; Chen Shun-cun; Liu Jing-sheng
 CORPORATE SOURCE: Guangzhou Institute of Respiratory Diseases, The First Affiliated Hospital, Guangzhou Medical College, Guangzhou 510120, China.
 SOURCE: Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases, (2003 Jun) Vol. 26, No. 6, pp. 358-61. Journal code: 8712226. ISSN: 1001-0939. L-ISSN: 1001-0939. China
 PUB. COUNTRY: (ENGLISH ABSTRACT)
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: Chinese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200311
 ENTRY DATE: Entered STN: 6 Aug 2003
 Last Updated on STN: 8 Nov 2003
 Entered Medline: 7 Nov 2003
 AB OBJECTIVE: The underlying mechanism by which nitric-oxide synthase (iNOS) gene transfer inhibits hypoxia-induced PSMCs proliferation remains unknown. The aim of this study is to investigate if iNOS gene transfer to PSMCs during hypoxia has any effect on cell cycle progression.
 METHODS: Using the cationic liposome mediation method , we transfected a recombinant pLNCX/iNOS vector into rat PSMCs. The instantaneous transgenic expression and the function of the recombinant protein were detected. Cell cycle analysis was performed by flow cytometry and cell proliferation assay by [(3)H] thymidine incorporation. The proteins involved in cell cycle control (P27 and P21) were determined by RT-PCR and flow cytometry.
 RESULTS: iNOS expression was detected in the transfected PSMCs. NO(2)(-) levels were increased in iNOS-transfected cells as compared to the untransfected cells. Expression of iNOS in rat PSMCs under hypoxia resulted in a delay in inhibition of DNA synthesis and cell cycle progression. The incorporation of [(3)H] thymidine in iNOS-transfected group (15,145 +/- 1,514) dpm was significantly lower than those in the hypoxia group (18,011 +/- 2,521) dpm (P < 0.01). The G(0)/G(1) cell cycle arrest rate in the iNOS-transfected group (67.8%) was significantly higher than those in the hypoxia group (46.8%) (P < 0.01). The protein level of P27 was down-regulated by hypoxia but not in iNOS-transfected cells under

hypoxia, and the level of the latter was similar to that under normoxia.

CONCLUSIONS: Pre-transfer of iNOS gene to PASCs under hypoxia inhibits cell proliferation via blocking P27 down-regulation, which is an important mechanism for the delay of cell cycle progression.

L7 ANSWER 33 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003386769 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12921555
TITLE: Specifics anti-tumor immunity induced by gene immunization with ectopic hCgbeta encoding gene.
AUTHOR: Wang Li-xin; Wu Jin; Guan Qing-dong; Xiong Si-dong
CORPORATE SOURCE: Shanghai Gene Immunization and Vaccine Research Center, Department of Immunology, Shanghai Medical College of Fudan University, Shanghai 200032, China.
SOURCE: Zhonghua zhong liu za zhi [Chinese journal of oncology], (2003 Jul) Vol. 25, No. 4, pp. 316-9.
Journal code: 7910681. ISSN: 0253-3766. L-ISSN: 0253-3766.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
Chinese
LANGUAGE: Priority Journals
FILE SEGMENT: 200503
ENTRY MONTH: Entered STN: 19 Aug 2003
ENTRY DATE: Last Updated on STN: 18 Dec 2003
Entered Medline: 17 Mar 2005
AB OBJECTIVE: To investigate the specific anti-tumor immunity induced by gene immunization with ectopic hCG encoding gene.

METHODS: BALB/c mice were immunized with plasmid TR421-hCgbeta coding for hCgbeta and mock DNA for 3 times at 3 weekly intervals. The level of specific anti-hCgbeta IgG antibody in the serum was determined by ELISA at the indicated time in the two groups. The growth inhibitory activity of the sera against tumor cells was examined in vitro by [(3)H]-Thymidine incorporation assay. Specific lympho-proliferation versus hCgbeta was detected by [(3)H]-Thymidine incorporation assay with hCgbeta protein or inactivated SP2/0-hCgbeta cells as specific stimulating antigen. Cytotoxic T lymphocyte (CTL) activity of the splenocytes derived from the immunized mice was measured by [(3)H]-Thymidine release assay. Protective assay was performed by subcutaneous inoculation of SP2/0-hCgbeta cells into the immunized mice. The weight and formation rate of the tumor were evaluated after challenge.

RESULTS: All mice immunized with plasmid TR421-hCgbeta developed high level of anti-hCgbeta antibodies, which could inhibit the growth of Hela cells and SP2/0-hCgbeta cells compared with the serum from animals immunized with mock DNA ($P < 0.05$). The high-level specific lympho-proliferation against hCgbeta protein or/and inactivated SP2/0-hCgbeta cells were shown in TR421-hCgbeta immunized mice, whereas no significant proliferative activity was found in mock DNA immunized animals ($P < 0.01$). A strong cytotoxic activity against SP2/0-hCgbeta in TR421-hCgbeta immunized mice was found. Inoculation of SP2/0-hCgbeta cells into the mice immunized with mock DNA developed large tumors within 25 days. But a marked reduction of tumor weight and formation rate was found after the tumor cells challenge in the mice immunized with TR421-hCgbeta plasmid DNA ($P < 0.01$).

CONCLUSION: The gene immunization of ectopic hCgbeta encoding gene, eliciting high-level of specific humoral and cellular immune responses,

could inhibit the growth of tumor cells harboring ectopic hCGbeta in vitro and in vivo.

L7 ANSWER 34 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003520358 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14520590
TITLE: [Cow milk-specific humoral and cellular immune response in infants with high risk of atopy under feeding a whey hydrolysate infant formula].
Kuhmilchspezifische humorale und zelluläre Immunantwort bei Säuglingen mit hohem Atopierisiko unter Ernährung mit einer Molke-Hydrolysatnahrung.
AUTHOR: Nentwich I; Pazdirkova A; Koberska I; Pokojcka E; Szepfalusi Z; Lokaj J
CORPORATE SOURCE: Institut der klinischen Immunologie und Allergologie, Masaryk-Universität in Brunn, Tschechien.
inentw@med.muni.cz
SOURCE: Klinische Padiatrie, (2003 Sep-Oct) Vol. 215, No. 5, pp. 275-9.
Journal code: 0326144. ISSN: 0300-8630. L-ISSN: 0300-8630.
PUB. COUNTRY: Germany; Federal Republic of
DOCUMENT TYPE: (COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 6 Nov 2003
Last Updated on STN: 17 Jan 2004
Entered Medline: 16 Jan 2004
AB BACKGROUND: Hypoallergenic infant formulas (HAF) were developed for atopy prevention in infants with high risk of atopy if these cannot be breastfed. HAF mount an antigen-specific immune response in infants. The aim of the study was to analyse the immune response in infants fed with a new infant formula based on a whey hydrolysate (HAF) and to compare it with that of exclusively breastfed controls.

PATIENTS AND METHODS: Plasma concentrations of cow milk-specific IgE were analysed in 94 infants with high risk of atopy, 44 were exclusively breastfed, 50 were fed with HAF. In addition, cow milk-specific IgG antibodies (26 breastfed, 30 fed with HAF) as well as proliferation of peripheral blood mononuclear cells to bovine beta-lactoglobulin (BLG) (41 breastfed, 47 fed with HAF) were tested. Specific IgE and IgG antibodies were determined using enzymeimmunoassay (Alastat). Cellular proliferation was measured using tritiated thymidine incorporation assay after 6 day stimulation with BLG.

RESULTS: Elevated IgE to cow milk antibodies (> 0.35 kU/L) were detected in two infants from the breastfed group and in one from the HAF-fed group. The plasma concentrations of milk specific IgG antibodies in HAF-fed infants were insignificantly higher than those in breastfed ones. No significant difference was found in bovine BLG-specific cell proliferation between both groups.

CONCLUSION: Concerning the properties investigated like antigenicity, allergenicity and immunogenicity, the extensively hydrolysed whey based hypoallergenic formula does not significantly differ from mother milk in 6 month-old infants with an increased atopy risk.

L7 ANSWER 35 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003136731 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12651233
 TITLE: Effects of angiotensin II and losartan on the growth and proliferation of hepatic stellate cells.
 AUTHOR: Zhang Yi-jun; Yang Xi-shan; Wu Ping-sheng; Li Xu; Zhang Xiao-feng; Chen Xiao-qing; Yu Zhong-xun
 CORPORATE SOURCE: Second Department of Gerontology, Guangzhou General Hospital of Guangzhou Command, Guangzhou 510010, China.
 SOURCE: Di 1 jun yi da xue xue bao = Academic journal of the first medical college of PLA, (2003 Mar) Vol. 23, No. 3, pp. 219-21, 227.
 Journal code: 9426110. ISSN: 1000-2588. L-ISSN: 1000-2588.
 PUB. COUNTRY: China
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200312
 ENTRY DATE: Entered STN: 25 Mar 2003
 Last Updated on STN: 16 Dec 2003
 Entered Medline: 15 Dec 2003

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
 AB OBJECTIVE: To investigate the effects of angiotensin II (AngII) and AT1a blocker losartan on growth and proliferation of rat hepatic stellate cells (HSCs).

METHODS: Rat HSCs were isolated, cultured and identified, followed by incubation with AngII or losartan at different concentrations. The cell growth and proliferation were assessed via cell counting and MTT assay, and the effects of the agents on HSC DNA synthesis evaluated by way of (3)H-thymidine incorporation ((3)H-TDR).

RESULTS: AngII (1×10^{-9}) to 1×10^{-7} mol/L stimulated HSC proliferation as demonstrated by cell counting, MTT assay and thymidine incorporation test ($P < 0.05$), but such effect was not observed at lower doses ($<1 \times 10^{-9}$ mol/L). Losartan had significant inhibitory effect on HSC growth at the concentration of 1×10^{-8} to 1×10^{-6} mol/L ($P < 0.05$), but not at lower doses ($<1 \times 10^{-8}$ mol/L). Co-stimulation of the cells with losartan and AngII did not result in a significant increase in cell number as compared with the control group ($P > 0.05$).

CONCLUSION: Rapid proliferation of rat HSCs occurs in response to AngII treatment, but is inhibited after AT1a receptor is blocked with the antagonist losartan.

L7 ANSWER 36 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2003139243 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12655439
 TITLE: Stimulation of intestinal epithelial restitution by prostaglandin E(1) analogues.
 AUTHOR: Hirata Kohji; Horie Toshiharu
 CORPORATE SOURCE: Department of Biopharmaceutics, Graduate School of Pharmaceutical Sciences, Chiba University, 1-33 Yayoi-cho, Inage-ku, 263-8522, Chiba, Japan.
 SOURCE: Cancer chemotherapy and pharmacology, (2003 Mar) Vol. 51, No. 3, pp. 216-20. Electronic Publication: 2003-02-26.
 Journal code: 7806519. ISSN: 0344-5704. L-ISSN: 0344-5704.
 PUB. COUNTRY: Germany; Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 26 Mar 2003
Last Updated on STN: 17 May 2003
Entered Medline: 16 May 2003

AB BACKGROUND: 5-Fluorouracil (5-FU) causes intestinal mucosal damage and malabsorption. We have recently reported that coadministration of 17 S,20-dimethyl- trans- lower right triangle (2)-prostaglandin E(1) (OP-1206), a stable synthetic analogue of prostaglandin E(1), with 5-FU to rats protects the small intestine from 5-FU-induced damage. Enterocyte proliferation would contribute to the restitution of the wounded intestinal mucosa. Thus, we investigated the effect of OP-1206 on the proliferation of rat jejunal crypt cells (IEC-6 cells) treated with 5-FU.

METHODS: Proliferation of IEC-6 cells was evaluated in terms of [(3)H]-thymidine incorporation and using the 3-(4,5-dimethyl-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Mucosal healing was assessed by measuring the speed of resealing across the denuded area of an IEC-6 cell monolayer.

RESULTS: OP-1206 stimulated [(3)H]-thymidine incorporation into subconfluent IEC-6 cells pretreated with 5-FU and increased the number of IEC-6 cells. AH23848B, an EP4 prostaglandin receptor antagonist, blocked the OP-1206-stimulated [(3)H]-thymidine incorporation into IEC-6 cells. The speed of resealing across the denuded area of a wounded IEC-6 cell monolayer was found to increase following treatment with OP-1206.

CONCLUSIONS: OP-1206 stimulated the proliferation of IEC-6 cells treated with 5-FU, indicating a possible mechanism for the protective effect of OP-1206 against 5-FU-induced damage to the small intestine. OP-1206 was shown to be active in intestinal mucosal healing.

L7 ANSWER 37 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003399874 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12938820
TITLE: Single exposure of mesothelial cells to glucose degradation products (GDPs) yields early advanced glycation end-products (AGEs) and a proinflammatory response.
AUTHOR: Welten Angelique G A; Schalkwijk Casper G; ter Wee Piet M; Meijer Sybren; van den Born Jacob; Beelen Robert J H
CORPORATE SOURCE: Department of Molecular Cell Biology, VU University Medical Center, Amsterdam, The Netherlands.
SOURCE: aga.welten.cell@med.vu.nl
SOURCE: Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis, (2003 May-Jun) Vol. 23, No. 3, pp. 213-21.
JOURNAL code: 8904033. ISSN: 0896-8608. L-ISSN: 0896-8608.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: (RESEARCH SUPPORT, NON-U.S. GOV'T)
ENTRY MONTH: Priority Journals
ENTRY DATE: 200401
ENTRY DATE: Entered STN: 27 Aug 2003
Last Updated on STN: 16 Jan 2004
Entered Medline: 15 Jan 2004

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: Fluids commonly used for peritoneal dialysis (PD) have a low pH and a high glucose content. Furthermore, heat sterilization of dialysis fluids degrades some of the glucose into glucose degradation products (GDPs), such as methylglyoxal (MGO) and 3-deoxyglucosone (3-DG). Mesothelial cells (MCs) form the first line in the peritoneal cavity and

are constantly exposed to these nonphysiological conditions. Since MCs play an important role in the regulation of inflammatory responses in the peritoneal cavity, we studied the kinetics of MC uptake of highly purified GDP species, along with their effect on various cellular biological and immunological parameters.

METHODS: Methylglyoxal and 3-DG were purified and added to MC cultures. Complexing to medium components or uptake by MCs was analyzed over time by HPLC of the culture supernatant and by immunocytochemistry of MCs for MGO-modified proteins. Furthermore, MCs were exposed to a single dose of MGO or 3-DG and analyzed for apoptosis, proliferation by MTT assay, and [3H]-thymidine incorporation. Incorporation of [35S]-methionine was determined in order to analyze de novo protein synthesis. Expression of the adhesion molecules intercellular adhesion molecule-1 (ICAM-1), CD44, and vascular cell adhesion molecule-1 (VCAM-1) was analyzed by cell-bound ELISA. Effects of MGO and 3-DG on cytokine production were also analyzed.

RESULTS: Substitution of MGO and 3-DG in culture medium resulted in a spontaneous decrease in MGO over time, whereas 3-DG levels decreased minimally. The concentration of these GDPs was more reduced in the presence of MCs, indicating binding to and/or uptake by MCs of these GDPs. Mesothelial cells that had been cultured in the presence of MGO showed positive staining with a monoclonal that specifically recognizes MGO-modified proteins, demonstrating complexing to mesothelial cellular proteins. Cell-bound ELISA showed a two- to three-fold induction of expression of VCAM-1 by MGO and 3-DG; the expression of ICAM-1 and CD44 was not changed. Mesothelial cells showed a twofold increase in interleukin (IL)-6 and IL-8 production after exposure to 3-DG. Furthermore, incubation with MGO and 3-DG induced apoptosis and reduced the proliferation of cells, but did not influence protein synthesis.

CONCLUSIONS: In the current report we demonstrate that MCs take up MGO and 3-DG and form early advanced glycation end-products. Upon short exposure to a single GDP, MCs react with enhanced cytotoxic damage and a proinflammatory response, evidenced by increased VCAM-1 expression and elevated production of IL-6 and IL-8.

L7 ANSWER 38 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003580091 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14659909
TITLE: A sensitive method for detecting proliferation of rare autoantigen-specific human T cells.
AUTHOR: Mannering Stuart I; Morris Jessica S; Jensen Kent P; Purcell Anthony W; Honeyman Margo C; van Endert Peter M; Harrison Leonard C
CORPORATE SOURCE: Autoimmunity and Transplantation Division, The Walter and Eliza Hall Institute, Royal Melbourne Hospital, Parkville, Victoria 3050, Australia. mannering@wehi.edu.au
SOURCE: Journal of immunological methods, (2003 Dec) Vol. 283, No. 1-2, pp. 173-83.
Journal code: 1305440. ISSN: 0022-1759. L-ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 23 Jan 2004
Entered Medline: 22 Jan 2004
OS.CITING REF COUNT: 14 There are 14 MEDLINE records that cite this record

AB The ability to measure proliferation of rare antigen-specific T cells among many bystanders is critical for the evaluation of cellular immune function in health and disease. T-cell proliferation in response to antigen has been measured almost exclusively by 3H-thymidine incorporation. This method does not directly identify the phenotype of the proliferating cells and is frequently not sufficiently sensitive to detect rare autoantigen-specific T cells. To overcome these problems, we developed a novel assay for antigen-specific human T-cell proliferation. Peripheral blood mononuclear cells (PBMC) were labelled with the fluorescent dye 5,6-carboxylfluorescein diacetate succinimidyl ester (CFSE) and cells that proliferated in response to antigen, with resultant reduction in CFSE intensity, were measured directly by flow cytometry. This assay was more sensitive than 3H-thymidine incorporation and detected the proliferation of rare antigen-specific CD4(+) T cells at 10-fold lower antigen concentrations. It also allowed the phenotype of the proliferating cells to be directly determined. Using the CFSE assay we were able to measure directly the proliferation of human CD4(+) T cells from healthy donors in response to the type 1 diabetes autoantigens glutamic acid decarboxylase (GAD) and proinsulin (PI).

L7 ANSWER 39 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003314885 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12844105
TITLE: Inability of vascular smooth muscle cells to proceed beyond S phase of cell cycle, and increased apoptosis in symptomatic carotid artery disease.
AUTHOR: Dhume Ashwini S; Agrawal Devendra K
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, NE 68178, USA.
SOURCE: Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter, (2003 Jul) Vol. 38, No. 1, pp. 155-61.
Journal code: 8407742. ISSN: 0741-5214. L-ISSN: 0741-5214.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 8 Jul 2003
Last Updated on STN: 30 Jul 2003
Entered Medline: 29 Jul 2003

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record

AB OBJECTIVE: Microemboli passing through the cerebral artery downstream from high-grade carotid artery stenosis produce transient ischemic symptoms and may result in stroke. Rupture of carotid artery plaque is the main source of microemboli in high-grade internal carotid artery stenosis. However, the mechanisms underlying plaque rupture are unclear. We hypothesized that vascular smooth muscle cells (VSMC) from plaque in patients with symptoms of carotid artery stenosis undergo increased apoptosis and decreased proliferation, compared with VSMC in patients without symptoms.

METHODS: VSMC were isolated by means of enzymatic dissociation from plaque removed at carotid endarterectomy in patients with symptoms of carotid artery stenosis, eg, hemispheric transient ischemic attacks, amaurosis fugax, or stroke, and patients with high-grade stenosis without symptoms. VSMC were cultured and immunostained with smooth muscle alpha-actin and caldesmon antibodies to ensure purity. TUNEL assay and annexin V labeling were performed to identify VSMC undergoing apoptosis.

Proliferation assay with [(3)H] thymidine incorporation was performed in VSMC stimulated with fetal bovine serum (FBS), and cell cycle profile was analyzed with DNA staining with Vindelov reagent.

RESULTS: We isolated VSMC from symptomatic plaque that showed gross ulceration, and asymptomatic plaque. Apoptosis, as measured with the TUNEL assay, in VSMC from symptomatic plaque was 5.45% +/- 0.8%, and in asymptomatic plaque was 1.20% +/- 0.2%. Annexin V labeling revealed that 26.8% +/- 3.8% cells were labeled for phosphatidylserine in VSMC in symptomatic plaque, compared with 4.8% +/- 0.3% cells in asymptomatic plaque. VSMC in asymptomatic plaque showed significantly increased uptake of [(3)H] thymidine at all concentrations of FBS, compared with symptomatic plaque. In the presence of 10% FBS, VSMC from asymptomatic plaque progressed through the S phase of the cell cycle, whereas significantly increased numbers of VSMC from symptomatic plaque were arrested in the S phase.

CONCLUSION: Increased numbers of VSMC from symptomatic plaque undergo apoptosis, compared with VSMC from asymptomatic plaque. This could be due to inability of VSMC from symptomatic plaque to progress beyond the S phase of the cell cycle. Decreased proliferation and increased loss of VSMC as a result of apoptosis in symptomatic plaque may result in plaque rupture, leading to development of symptoms.

L7 ANSWER 40 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003470556 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14532719
TITLE: Role of hepatic stellate cells in the angiogenesis of hepatoma.
AUTHOR: Jung Jun-Oh; Gwak Geum-Youn; Lim Young-Suk; Kim Chung Yong; Lee Hyo Suk
CORPORATE SOURCE: Department of Internal Medicine, Liver Research Institute, Seoul National University College of Medicine, Jongno-gu, Seoul, Korea.
SOURCE: The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi, (2003 Aug) Vol. 42, No. 2, pp. 142-8. Journal code: 101189416. ISSN: 1598-9992. L-ISSN: 1598-9992.
PUB. COUNTRY: Korea
DOCUMENT TYPE: (ENGLISH ABSTRACT)
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: Korean
ENTRY MONTH: Priority Journals
ENTRY DATE: 200404
Entered STN: 9 Oct 2003
Last Updated on STN: 16 Apr 2004
Entered Medline: 15 Apr 2004
AB BACKGROUND/AIMS: Hepatic stellate cells (HSCs) in the hepatocellular carcinoma are responsible for tumor encapsulation as a host defense mechanism. Recently, it was suggested that HSCs might play an important role in hepatic angiogenesis. Thus, HSCs in the HCC may be involved in tumor angiogenesis and pathogenesis of hepatic carcinogenesis. The purpose of this study was to examine the involvement of activated HSCs in the angiogenesis of hepatoma.

METHODS: We investigated the effect of human HSC conditioned medium (CM) on the endothelial cell proliferation with or without stimulation of HepG2 CM, using [3H] thymidine incorporation assay. Additionally, we investigated the effect of HepG2 CM on HSCs proliferation and messenger RNA (mRNA) expression of various pro-angiogenic factors such as interleukin 8 (IL-8),

basic fibroblast growth factor (bFGF), and vascular endothelial growth factor (VEGF) in HSCs.

RESULTS: HSC CM caused a significant increase in DNA synthesis in human umbilical vein endothelial cells (HUVEC). The endothelial proliferation effect of HSCs was augmented by HepG2 CM. HepG2 CM significantly increased HSCs proliferation and stimulated IL-8 and bFGF mRNA expression in HSCs.

CONCLUSIONS: HSCs promote endothelial proliferation through various soluble factors. The soluble factors secreted in HepG2 stimulate HSC proliferation and up-regulate mRNA expression of proangiogenic factors. This result suggests that HSCs may play an important role in the angiogenesis of hepatoma.

L7 ANSWER 41 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003200357 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12667670
TITLE: Flow cytometric analysis of T cell proliferation in a mixed lymphocyte reaction with dendritic cells.
AUTHOR: Nguyen Xuan Duc; Eichler Hermann; Dugrillon Alex; Piechaczek Christoph; Braun Michael; Kluter Harald
CORPORATE SOURCE: Institute of Transfusion Medicine and Immunology, Red Cross Blood Service of Baden-Wurtemberg - Hessen, Germany.
SOURCE: x.nguyen@blutspende.de
JOURNAL OF IMMUNOLOGICAL METHODS, (2003 Apr 1)
Vol. 275, No. 1-2, pp. 57-68.
JOURNAL CODE: 1305440. ISSN: 0022-1759. L-ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
(IN VITRO)
JOURNAL; ARTICLE; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 24 May 2003
Entered Medline: 23 May 2003

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB BACKGROUND: Dendritic cells (DCs) are the most potent antigen-presenting cells. They can be generated in vitro from CD14+ cells, and also from CD34+ progenitor cells. Although T cell proliferation using [3H] thymidine incorporation assay has been used widely to check DC function, this technique only provides limited information about the T cell proliferation. Here, we describe a novel method for quantitative analysis of T cell proliferation using flow cytometry.

MATERIALS AND METHODS: DCs were generated from CD14+ cells from six healthy blood donors. Monocytes were isolated using positive selection with magnetic cell sorting (MACS) and then cultured with IL-4, GM-CSF, IL-1beta, IL-6, TNF-alpha and PGE(2) to yield fully mature DCs. Allogeneic naive T lymphocytes with known mismatches in HLA classes I and II were cocultured with DCs. Naive T cells without DC stimulation served as negative controls. T cells were harvested on days 0, 3, 5, 7, 9, 11 and analysed by flow cytometry. CD3-ECD and CD4-fluorescein isothiocyanate (FITC) or CD8-FITC antibodies were used to distinguish T cell subsets, whereas T cell activation was measured by assessment of HLA-DR, CD45RO, CD25 and CD71 expression. For T cell quantification, fluorescent microparticles were used. Dead cells were excluded with 7-AAD. The bromodeoxyridine (BrdU)-incorporation ELISA procedure was also performed in order to compare with the T cell proliferation assay with

regard to absolute cell counts and CD71 expression.

RESULTS: The initial T cell concentration on day 1 was 203.9+/-39.7 (173-265) CD3+/CD4+ cells/micro l and 184.5+/-41.6 (148-260) CD3+/CD8+ cells/micro l. The maximal T cell proliferation was recorded on day 7 with a five- to tenfold T cell expansion which resulted in 1994.9+/-383 (1446-2404) CD3+/CD4+ cells/micro l and 944+/-303.7 (560-1483) CD3+/CD8+ cells/micro l. Furthermore, activation markers of both cell lineages were upregulated and reached maxima on days 7 (CD71) and 9 (CD25, HLA-DR). T cell count/micro l as well as CD71 expression both correlated significantly with BrdU incorporation.

CONCLUSION: Flow cytometric analysis permits simple, precise and rapid quantification of T cell proliferation in a mixed lymphocyte reaction with DCs. Activation, proliferation and cell viability can be simultaneously determined. CD71 is particularly well suited as an activation marker for the simultaneous measurement of T cell proliferation. Thus, specific T cell subsets involved in antigen-specific proliferation can be evaluated in detail.

L7 ANSWER 42 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003381106 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12916303
TITLE: Experimental study of proliferation of Schwann cells cultured with ginsenoside Rb1.
AUTHOR: Wu Hay-tong; Chen Xiao-xiang; Xiong Liang-jian
CORPORATE SOURCE: Department of Orthopedics and Traumatology, Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong, P. R. China.
SOURCE: Zhongguo xiu fu chong jian wai ke za zhi = Zhongguo xiufu chongjian waikexue zazhi = Chinese journal of reparative and reconstructive surgery, (2003 Jan) Vol. 17, No. 1, pp. 26-9.
Journal code: 9425194. ISSN: 1002-1892. L-ISSN: 1002-1892.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 15 Aug 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 17 Dec 2003
AB OBJECTIVE: To investigate the effects of Ginsenoside Rb1 on the proliferation of Schwann cell cultured.
METHODS: The sciatic nerve from SD rats was cultured in vitro; 10 micrograms/ml, 20 micrograms/ml, 200 micrograms/ml and 1 mg/ml Ginsenoside Rb1 was applied on the fifth day of culture. The proliferation of Schwann cells of sciatic nerves was determined in different time by MTT assay and thymidine incorporation assay.
RESULTS: 10 micrograms/ml of Ginsenoside Rb1 significantly induced Schwann cell proliferation better than DMEM cell culture medium, but higher concentrations of Ginsenoside Rb1 at 1 mg/ml significantly inhibited the proliferation of Schwann cells, whereas 200 micrograms/ml of Ginsenoside Rb1 had similar effects to DMEM culture medium.
CONCLUSION: Ginsenoside Rb1 at the optimal concentration is effective on inducing the proliferation of Schwann cells, but at higher concentration is cytotoxic for Schwann cells.

L7 ANSWER 43 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2002707318 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12468797
 TITLE: Cerebral capillary endothelial cell mitogenesis and morphogenesis induced by astrocytic epoxyeicosatrienoic Acid.
 AUTHOR: Zhang Chenyang; Harder David R
 CORPORATE SOURCE: Cardiovascular Research Center, Department of Physiology, Medical College of Wisconsin, Milwaukee, USA.
 CONTRACT NUMBER: P01 HL 59996 (United States NHLBI NIH HHS)
 SOURCE: Stroke; a journal of cerebral circulation, (2002 Dec) Vol. 33, No. 12, pp. 2957-64.
 Journal code: 0235266. E-ISSN: 1524-4628. L-ISSN: 0039-2499.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200301
 ENTRY DATE: Entered STN: 17 Dec 2002
 Last Updated on STN: 10 Jan 2003
 Entered Medline: 9 Jan 2003
 OS.CITING REF COUNT: 10 There are 10 MEDLINE records that cite this record
 AB UNLABELLED: Background and Purpose- Epoxyeicosatrienoic acids (EETs) are products of cytochrome P450 epoxidation of arachidonic acid. We have previously demonstrated that astrocyte-conditioned medium induced mitogenesis in brain capillary endothelial cells. The goals of the present studies are to further define the mechanism through which this can occur and to confirm that EETs are derived from astrocytes, through which astrocytic activity can regulate cerebral angiogenesis in response to neuronal activation.
 METHODS: Astrocytes and cerebral capillary endothelial cells in primary cultures were cocultured to examine the interaction of the 2 cell types. We used multiple immunohistochemical techniques to characterize the multicellular nature of the capillaries, which is not simply an artifact related to the culture conditions. The mitogenic effect of EETs was determined by (3)H-thymidine incorporation and cell proliferation assay. Endothelial tube formation was examined in vitro and in vivo with the use of a reconstituted basement membrane (Matrigel) assay.
 RESULTS: In cocultures of astrocytes and capillary endothelium, we observed morphological changes in both cell types such that each assumed certain physiological characteristics, ie, endothelial networks and astrocytes with "footlike" projections as well as intermittent gap junctions forming within the endothelial cells. EETs from astrocytes as well as synthetic EETs promoted mitogenesis of endothelial cells, a process sensitive to inhibition of tyrosine kinase with genistein. Treatments with exogenous EETs were sufficient for endothelial cells to differentiate into capillary-like structures in culture as well as in vivo in a Matrigel matrix.
 CONCLUSIONS: The 2 major conclusions from these data are that astrocytes may play an important role in regulating angiogenesis in the brain and that cytochrome P450-derived EETs from astrocytes are mitogenic and angiogenic.

L7 ANSWER 44 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2002737708 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12499878
TITLE: Characterization of fibroblasts from rejecting tissue: the hyaluronan production is increased.
AUTHOR: Hellkvist Josefin; Tufveson Gunnar; Gerdin Bengt; Johnsson Cecilia
CORPORATE SOURCE: Department of Transplantation Surgery, University Hospital, Uppsala, Sweden.
SOURCE: Transplantation, (2002 Dec 27) Vol. 74, No. 12, pp. 1672-7.
JOURNAL CODE: 0132144. ISSN: 0041-1337. L-ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 27 Dec 2002
Last Updated on STN: 17 Jan 2003
Entered Medline: 16 Jan 2003

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: Interstitial edema of rejecting tissue can be partly attributed to the local accumulation of hyaluronan, which has strong water-binding capacity. The aim of the present study was to isolate fibroblasts from rejecting tissue and compare them, in terms of hyaluronan production and proliferation rate, with fibroblasts obtained from nontransplanted tissue. Furthermore, the fibroblast response to various cytokines involved in the rejection process was studied.

METHODS: Fibroblasts were isolated from normal rat heart tissue and from cardiac allografts undergoing rejection. The various preparations were characterized with regard to hyaluronan production (radiometric assay) and cell proliferation (H-thymidine incorporation). In addition, the effects of tumor necrosis factor (TNF)-alpha, interferon (IFN)-gamma, and interleukin (IL)-2 on these parameters were studied.

RESULTS: Fibroblasts isolated from rejecting hearts displayed strongly up-regulated hyaluronan production and proliferation rate as compared with fibroblasts obtained from normal tissue. In the presence of TNF-alpha, the proliferation of nonconfluent cells was augmented, whereas in confluent cultures of fibroblasts from rejecting tissue, the proliferation was inhibited. IFN-gamma stimulated both hyaluronan secretion and proliferation in confluent fibroblasts from rejecting hearts but had no effect on fibroblasts from normal tissue. IL-2, finally, reduced the hyaluronan production of nonconfluent cells.

CONCLUSIONS: The activation of fibroblasts is increased in rejecting tissue. As a result, the hyaluronan concentration is elevated which, in vivo, contributes to the formation of an interstitial edema and a subsequently increased tissue pressure. Several cytokines present at rejection are involved also in the regulation of fibroblast activity.

L7 ANSWER 45 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002616076 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12371966
TITLE: P2 receptor antagonist PPADS inhibits mesangial cell proliferation in experimental mesangial proliferative glomerulonephritis.
AUTHOR: Rost Sylvia; Daniel Christoph; Schulze-Lohoff Eckhard; Baumert Hans G; Lambrecht Gunter; Hugo Christian
CORPORATE SOURCE: Division of Nephrology, University of Erlangen-Nurnberg, Erlangen, Germany.

SOURCE: Kidney international, (2002 Nov) Vol. 62, No. 5,
pp. 1659-71.
Journal code: 0323470. ISSN: 0085-2538. L-ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 10 Oct 2002
Last Updated on STN: 13 Mar 2003
Entered Medline: 12 Mar 2003

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
AB BACKGROUND: Although extracellular nucleotides have been shown to confer mitogenic effects in cultured rat mesangial cells through activation of purinergic P2 receptors (P2Y receptors), thus far the in vivo relevance of these findings is unclear. Virtually all cells and in particular the dense granules of platelets contain high levels of nucleotides that are released upon cell injury or platelet aggregation. In experimental mesangial proliferative glomerulonephritis in the rat (anti-Thyl model), mesangiolysis and glomerular platelet aggregation are followed by a pronounced mesangial cell (MC) proliferative response leading to glomerular hypercellularity. Therefore, we examined the role of extracellular nucleotides and their corresponding receptors in nucleotide-stimulated cultured mesangial cells and in inflammatory glomerular disease using the P2 receptor antagonist PPADS.

METHODS: The effects of PPADS on nucleotide- or fetal calf serum (FCS)-stimulated proliferation of cultured MC were measured by cell counting and [3H]thymidine incorporation assay. After induction of the anti-Thyl model, rats received injections of the P2-receptor antagonist PPADS at different doses (15, 30, 60 mg/kg BW). Proliferating mesangial and non-mesangial cells, mesangial cell activation, matrix accumulation, influx of inflammatory cells, mesangiolysis, microaneurysm formation, and renal functional parameters were assessed during anti-Thyl disease. P2Y-mRNA and protein expression was assessed using RT-PCR and real time PCR, Northern blot analysis, in situ hybridization, and immunohistochemistry.

RESULTS: In cultured mesangial cells, PPADS inhibited nucleotide, but not FCS-stimulated proliferation in a dose-dependent manner. In the anti-Thyl model, PPADS specifically and dose-dependently reduced early (day 3), but not late (day 8), glomerular mesangial cell proliferation as well as phenotypic activation of the mesangium and slightly matrix expansion. While no consistent effect was obtained in regard to the degree of mesangiolysis, influx of inflammatory cells, proteinuria or blood pressure, PPADS treatment increased serum creatinine and urea in anti-Thyl rats. P2Y receptor expression (P2Y2 and P2Y6) was detected in cultured MC and isolated glomeruli, and demonstrated a transient marked increase during anti-Thyl disease.

CONCLUSION: These data strongly suggest an in vivo role for extracellular nucleotides in mediating early MC proliferation after MC injury.

L7 ANSWER 46 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002388236 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12136906
TITLE: Autoimmunity against YKL-39, a human cartilage derived protein, in patients with osteoarthritis.
AUTHOR: Tsuruha Jun-Ichiro; Masuko-Hongo Kayo; Kato Tomohiro;

Sakata Masahiro; Nakamura Hiroshi; Sekine Taichi; Takigawa Masaharu; Nishioka Kusuki
 CORPORATE SOURCE: Rheumatology, Immunology and Genetics Program, Institute of Medical Science, St Marianna University School of Medicine, Kawasaki, Japan.
 SOURCE: The Journal of rheumatology, (2002 Jul) Vol. 29, No. 7, pp. 1459-66.
 Journal code: 7501984. ISSN: 0315-162X. L-ISSN: 0315-162X.
 PUB. COUNTRY: Canada
 DOCUMENT TYPE: (COMPARATIVE STUDY)
 Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200301
 ENTRY DATE: Entered STN: 25 Jul 2002
 Last Updated on STN: 25 Jan 2003
 Entered Medline: 24 Jan 2003

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
 AB OBJECTIVE: Our previous study revealed that some patients with rheumatoid arthritis (RA) possessed autoantibodies to YKL-39, a cartilage related protein. We investigated whether patients with osteoarthritis (OA) also displayed autoimmunity to YKL-39.

METHODS: Autoantibodies to recombinant YKL-39 as well as human cartilage glycoprotein-39 were detected by ELISA and Western blotting. The tested serum samples were derived from 117 patients with OA, 94 patients with RA, and 2 groups of 50 arthropathy-free healthy donors who matched the OA and RA groups for age and sex. We determined autoepitopes on YKL-39 using 3 overlapping fragments of YKL-39 (designated F1, F2, F3). T cell proliferation response to YKL-39 was analyzed using the 3H-thymidine incorporation assay.

RESULTS: Autoantibodies to YKL-39 were detected in 13 (11.1%) patients with OA and 11 (11.8%) with RA. In the epitope mapping, all the 3 fragments of YKL-39 were found to carry autoepitopes, but F1 was recognized most frequently. Proliferative responses of peripheral blood mononuclear cells against YKL-39 were detected in 6 (46%) of the 13 OA patients who were positive for the anti-YKL-39 autoantibodies and in 2 (17%) of the 11 antibody positive RA patients.

CONCLUSION: These results show that autoimmunity to YKL-39 in patients with OA was present at equal or somewhat higher frequency than in patients with RA. The cellular and humoral immune responses to YKL-39 may be involved in the pathological process of OA as well as RA.

L7 ANSWER 47 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2002475477 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12237284
 TITLE: The effects of malignant transformation on susceptibility of human urothelial cells to CD40-mediated apoptosis.
 AUTHOR: Bugajska Urszula; Georgopoulos Nikolaos T; Southgate Jennifer; Johnson Peter W M; Graber Pierre; Gordon John; Selby Peter J; Trejdosiewicz Ludwik K
 CORPORATE SOURCE: Cancer Research UK, Clinical Centre, St. James's University Hospital, Leeds, UK.
 SOURCE: Journal of the National Cancer Institute, (2002 Sep 18) Vol. 94, No. 18, pp. 1381-95.
 Journal code: 7503089. ISSN: 0027-8874. L-ISSN: 0027-8874.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 19 Sep 2002
Last Updated on STN: 8 Oct 2002
Entered Medline: 4 Oct 2002

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: The tumor necrosis factor (TNF) superfamily of ligands and receptors mediates immune cell survival. Some members possess a death domain, a protein motif that functions to transmit apoptotic signals, whereas others, such as CD40, do not. CD40 is expressed by both normal and malignant epithelial cells. To investigate the functional significance of this expression, we studied the effects of ligation of CD40, Fas, and TNF receptors (TNFRs) on the proliferation and survival of normal and malignant human urothelial cells and urothelial cells with disabled p53 function.

METHODS: Normal and malignant human urothelial cells were cultured with soluble TNF family agonists (CD40 ligand [CD40L], TNF-alpha, anti-Fas antibody, or cocultured with mouse fibroblasts stably transfected with plasmids that caused the cells to constitutively express CD40L or CD32; cell proliferation was estimated by an [(3)H] thymidine incorporation assay, and apoptosis was determined by Annexin V staining and by a DNA fragmentation assay. Messenger RNA levels for CD40 and potential downstream effector molecules were quantified by polymerase chain reaction-based and ribonuclease protection assays, respectively, and nuclear factor (NF) kappaB nuclear translocation was detected by immunofluorescence. All statistical tests were two-sided.

RESULTS: Soluble trimeric CD40L inhibited the growth of normal and malignant urothelial cells but did not induce apoptosis. Cell surface-presented CD40L induced massive apoptosis in CD40-positive transitional cell carcinoma cells but not in normal urothelial cells. Normal cells underwent CD40L-mediated apoptosis only in the presence of other TNFR agonists. An agonistic anti-CD40 antibody presented on the surface of CD32-transfected fibroblasts also induced apoptosis in transitional cell carcinoma cells and in normal urothelial cells. Apoptotic responses of tumor (but not normal) cells to soluble agonists were enhanced by blocking protein synthesis. Karyotypically normal urothelial cells with disabled p53 function underwent apoptosis during coculture with CD40L-expressing fibroblasts alone but were not additionally sensitive to additional TNFR agonists.

CONCLUSIONS: Susceptibility to CD40 ligation-induced apoptosis may be a novel mechanism for eliminating neoplastically transformed urothelial cells. Loss of CD40 expression may be an important adaptive mechanism for transitional cell carcinoma development and progression.

L7 ANSWER 48 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002245049 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11984520
TITLE: Critical role of caspases in the regulation of apoptosis and proliferation of mucosal T cells.
AUTHOR: Sturm Andreas; Mohr Susanne; Fiocchi Claudio
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine, University Hospital of Cleveland, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106-4952, USA.
CONTRACT NUMBER: DK30399 (United States NIDDK NIH HHS)
DK50984 (United States NIDDK NIH HHS)
SOURCE: Gastroenterology, (2002 May) Vol. 122, No. 5, pp.

1334-45.
Journal code: 0374630. ISSN: 0016-5085. L-ISSN: 0016-5085.
United States
PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE)
DOCUMENT TYPE: (RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 2 May 2002
Last Updated on STN: 28 May 2002
Entered Medline: 23 May 2002

OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record

AB BACKGROUND & AIMS: Caspases are critical mediators of apoptosis and

proliferation of peripheral blood T cells (PBT), but their role in lamina propria T cells (LPT), a cell population highly susceptible to apoptosis, has not been explored.

METHODS: RA(+), RO(+) PBT, and LPT were activated with CD3, CD2, and CD28 antibodies, and caspase activity, apoptosis, and proliferation were measured by a fluorometric assay, DNA content, and thymidine incorporation, respectively. Levels of FLIP, an endogenous inhibitor of caspase 8, were measured by immunoblotting.

RESULTS: In RA(+) and RO(+) PBT, activation leads to significant increase of caspase activity but not cell death, whereas in LPT a lower elevation of caspase activity was followed by a marked degree of apoptosis. Based on the results of its inhibition, caspase 8 seemed to be essential for LPT apoptosis but, in contrast to RA(+) PBT, had no effect on proliferation. In addition, compatible with their differential susceptibility to apoptosis, levels of FLIP were lower in LPT than PBT.

CONCLUSIONS: The high susceptibility of LPT to apoptosis is associated with a distinct regulation of caspase 8 activity, which seems to reflect their mucosal origin rather than simply their memory status. This unique behavior may allow proper control of mucosal T-cell proliferation while still permitting elimination by apoptosis in the face of excessive antigenic pressure.

L7 ANSWER 49 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002717588 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12478891
TITLE: Inhibition of activator protein-1 on the growth of gastric cancer by octreotide.
AUTHOR: Wang Chun-hui; Tang Cheng-wei
CORPORATE SOURCE: Department of Gastroenterology, West China Hospital of Sichuan University, Chengdu 610041, P. R. China.
SOURCE: Ai zheng = Aizheng = Chinese journal of cancer, (2002 Aug) Vol. 21, No. 8, pp. 850-4.
Journal code: 9424852. ISSN: 1000-467X. L-ISSN: 1000-467X.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 18 Dec 2002
Last Updated on STN: 28 Jan 2003
Entered Medline: 27 Jan 2003
AB BACKGROUND & OBJECTIVE: Somatostatin is a multi-functional neuropeptide.

Somatostatin and its analogues are able to inhibit the growth of neuroendocrine tumors and some gastrointestinal tumors. However, the effect of octreotide on growth of gastric carcinoma is still unknown. This study was designed to explore the mechanism of the effect of octreotide on growth of gastric cancer.

MATERIAL & METHODS: SGC-7901 cells were treated with octreotide at different concentrations for 24 hours. Proliferation of SGC-7901 cells was measured by ³H-thymidine incorporation assay. The nude mice bearing human stomach carcinoma were treated by octreotide for eight weeks. The c-Fos and extracellular signal-regulated protein kinase (ERK) protein expression levels were examined in SGC-7901 cells and carcinoma tissue by immunohistochemistry and immunoblotting. Activator protein-1 (AP-1) binding activity was detected by electrophoretic mobility shift assay (EMSA).

RESULTS: ³H-thymidine incorporation into SGC-7901 cells was significantly decreased by octreotide and showed concentration-dependent. Octreotide could significantly inhibit the growth of orthotopical implanted gastric cancer, the inhibition rate for tumors was 62.3%. The c-Fos and ERK-1/ERK-2 proteins were decreased in the nude mice carcinoma tissues and SGC-7901 gastric carcinoma cells which treated with octreotide by immunohistochemistry or immunoblotting analysis. Moreover, the fetal calf serum (FCS) stimulated AP-1 binding activity on gastric cancer cell and the somatostatin analogue octreotide could inhibit this response efficiently.

CONCLUSION: Octreotide inhibits not only ERK-1/ERK-2 and c-Fos expressions but also AP-1 binding activity, which result in inhibition to proliferation of gastric carcinoma cell.

L7 ANSWER 50 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002317115 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12060528
TITLE: Effect of *Misgurnus anguillicaudatus* polysaccharide on immune responses of splenocytes in mice.
AUTHOR: Qin Chuan-Guang; Huang Kai-Xun; Xu Hui-Bi
CORPORATE SOURCE: Pharmaceutical Institute, Huazhong University of Science and Technology, Wuhan 430074, China.
SOURCE: Acta pharmacologica Sinica, (2002 Jun) Vol. 23, No. 6, pp. 534-8.
Journal code: 100956087. ISSN: 1671-4083. L-ISSN: 1671-4083.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 13 Jun 2002
Last Updated on STN: 11 Dec 2002
Entered Medline: 16 Sep 2003
AB AIM: To investigate the effect of *Misgurnus anguillicaudatus* polysaccharides (MAP) on immune responses of splenocytes in mice.
METHODS: T lymphocyte proliferation (TLP) was measured by [³H]thymidine incorporation assay
. Cytotoxic T lymphocyte (CTL) cytotoxicity and natural killer (NK) activity were determined by release of radioactive chromium [⁵¹Cr] from pre-labeled target cells.
RESULTS: MAP 5 and 10 mg . kg⁻¹ . d⁻¹, ip for 7 d, could increase TLP,

enhance the cytotoxicity of CTL and NK cells, and antagonize the effect of concanavalin A (ConA) on TLP suppressed by cyclophosphamide (CP). Inhibitory rates of CTL cytotoxicity were decreased from 51.4 % in CP control mice to 18.2 % and 35.1 % in MAP-treated CP mice, respectively. Furthermore, administration of MAP 10 and 20 mg . kg⁻¹ . d⁻¹, ip for 7 d, restored the reduced NK cell cytotoxicity caused by CP administration in mice.

CONCLUSION: MAP has protective effect on augmenting T-cell-mediated immunity and NK activity in normal and CP-treated mice.

L7 ANSWER 51 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002304364 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12046072
TITLE: The promoting molecular mechanism of alpha-fetoprotein on the growth of human hepatoma Bel7402 cell line.
AUTHOR: Li Meng-Sen; Li Ping-Feng; He Shi-Peng; Du Guo-Guang; Li Gang
CORPORATE SOURCE: Department of Biochemistry, Hainan Medical College, Hainan, China.
SOURCE: World journal of gastroenterology : WJG, (2002 Jun) Vol. 8, No. 3, pp. 469-75.
Journal code: 100883448. ISSN: 1007-9327. L-ISSN: 1007-9327.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 5 Jun 2002
Last Updated on STN: 7 Aug 2002
Entered Medline: 6 Aug 2002

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB AIM: The goal of this study was to characterize the AFP receptor, its possible signal transduction pathway and its proliferative functions in human hepatoma cell line Bel 7402.

METHODS: Cell proliferation enhanced by AFP was detected by MTT assay, 3H-thymidine incorporation and S-stage percentage of cell cycle analysis. With radioactive labeled 125I-AFP for receptor binding assay; cAMP accumulation, protein kinase A activity were detected by radioactive immunosorbent assay and the change of intracellular free calcium (Ca²⁺) was monitored by scanning fluorescence intensity under TCS-NT confocal microscope. The expression of oncogenes N- ras, p 53, and p21(ras) in the cultured cells in vitro were detected by Northern blotting and Western blotting respectively.

RESULTS: It was demonstrated that AFP enhanced the proliferation of human hepatoma Bel 7402 cell in a dose dependent fashion as shown in MTT assay, (3)H-thymidine incorporation and S-phase percentage up to 2-fold. Two subtypes of AFP receptors were identified in the cells with Kds of 1.3 x 10⁻⁹mol.L⁻¹ and 9.9 x10⁻⁸mol. (-1)L respectively. Pretreatment of cells with AFP resulted in a significant increase (625%) in cAMP accumulation. The activity of protein kinase A activity were increased up to 37.5, 122.6, 73.7 and 61.2% at treatment time point 2, 6, 12 and 24 hours. The level of intracellular calcium were elevated after the treatment of alpha-fetoprotein and achieved to 204% at 4 min. The results also showed that AFP(20mg.L⁻¹) could upregulate the expression of N- ras oncogenes and p 53 and p21(ras) in Bel 7402 cells. In the later case, the alteration were 81.1% (12h) and

97.3%(12h) respectively compared with control.

CONCLUSION: These results demonstrate that AFP is a potential growth factor to promote the proliferation of human hepatoma Bel 7402 cells. Its growth-regulatory effects are mediated by its specific plasma membrane receptors coupled with its transmembrane signaling transduction through the pathway of cAMP-PKA and intracellular calcium to regulate the expression of oncogenes.

L7 ANSWER 52 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002366872 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110005
TITLE: Activin A: an autocrine regulator of cell growth and differentiation in renal proximal tubular cells.
AUTHOR: Maeshima Akito; Nojima Yoshinisa; Kojima Itaru
CORPORATE SOURCE: Institute for Molecular & Cellular Regulation, Gunma University, Maebashi, Japan.
SOURCE: Kidney international, (2002 Aug) Vol. 62, No. 2, pp. 446-54.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 14 Jan 2003
Entered Medline: 13 Jan 2003
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB BACKGROUND: Activin A is involved in tubular regeneration after ischemia/reperfusion injury. The present study was conducted to examine the role of activin A in cell growth, apoptosis and differentiation of tubular cells.

METHODS: We performed cell proliferation assays (MTT assay, [3H]-thymidine incorporation) and apoptosis detection assays (nuclear staining, DNA ladder formation, TUNEL staining) using LLC-PK1 cells. Expression of activin and activin receptor in LLC-PK1 cells also were examined by real-time polymerase chain reaction (PCR) and immunostaining. Stable cell lines expressing the truncated type II activin receptor were generated and the phenotype of these cells was analyzed.

RESULTS: Activin A inhibited DNA synthesis and cell growth in a dose-dependent manner and induced apoptosis in LLC-PK1 cells. The expression level of mRNA for the activin betaA subunit was markedly increased when the growth was stimulated. The expression of the type II activin receptor was observed in LLC-PK1 cells. The growth rate of cells expressing dominantly negative activin receptor was significantly faster than that of non-transfected cells. The expression level and pattern of cytokeratin and vimentin in these cells were quite different compared to non-transfected cells. When cultured in collagen gel, these cells formed multiple processes, which was not observed in non-transfected cells. Finally, the expression of Pax-2 was markedly elevated in these cells.

CONCLUSIONS: Activin A acts as an autocrine inhibitor of cell growth, an inducer of apoptosis, and an important modulator of differentiation in cultured proximal tubular cells.

L7 ANSWER 53 OF 188 MEDLINE on STN

ACCESSION NUMBER: 2002618038 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12207582
 TITLE: Cytokine production in nickel-sensitized individuals analysed with enzyme-linked immunospot assay: possible implication for diagnosis.
 AUTHOR: Jakobson E; Masjedi K; Ahlborg N; Lundeborg L; Karlberg A-T; Scheynius A
 CORPORATE SOURCE: Occupational Dermatology, National Institute for Working Life, Stockholm, Sweden.
 SOURCE: The British journal of dermatology, (2002 Sep) Vol. 147, No. 3, pp. 442-9.
 Journal code: 0004041. ISSN: 0007-0963. L-ISSN: 0007-0963.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200211
 ENTRY DATE: Entered STN: 12 Oct 2002
 Last Updated on STN: 13 Dec 2002
 Entered Medline: 22 Nov 2002

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
 AB BACKGROUND: Patients with suspected allergic contact dermatitis still have to undergo patch testing for a correct diagnosis. As this has several disadvantages there is a need for additional methods, preferentially those that can be performed in vitro. Objectives To investigate the possibility of diagnosing contact allergy to nickel (Ni2+) using the enzyme-linked immunospot (ELISpot) assay that allows the analysis of cytokines at a single-cell level in ex vivo activated peripheral blood mononuclear cells (PBMC).

METHODS: Eleven female patients and nine age- and sex-matched healthy volunteers participated in the study. All patients had a history of nickel allergy and a positive patch test reaction to NiSO4, while the controls' test was negative. PBMC were cultured in the presence or absence of NiCl2. Cell proliferation was measured with [3H] thymidine incorporation, and the number of cytokine-producing cells analysed with the ELISpot assay.

RESULTS: The proliferative response of PBMC to Ni2+, expressed as stimulation index, was significantly higher in the nickel-allergic patients than in the control group. Using the ELISpot assay, we found that PBMC from nickel-allergic individuals responded to Ni2+ with significantly greater production of interleukin (IL)-4, IL-5, IL-13 and interferon-gamma, but not IL-12, compared with the healthy controls. The number of IL-4- and IL-5-producing cells correlated with the number of IL-13-producing cells in the nickel-allergic patients, but Ni2+-induced PBMC proliferation did not correlate with the number of cytokine-producing cells for any of the cytokines tested.

CONCLUSIONS: Our results indicate that the ELISpot assay could be a tool in the discrimination between nickel-allergic and non-allergic individuals.

L7 ANSWER 54 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2003081195 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12443579
 TITLE: Effects of Ginsenoside Rb1 on proliferation of Schwann cells in culture.
 AUTHOR: Hu Xitang; Chen Xiaoxiang; Xiong Liangjian
 CORPORATE SOURCE: Department of Orthopaedics and Traumatology, Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong.

haytongwu@cuhk.edu.hk
SOURCE: Chinese journal of traumatology = Zhonghua chuang shang za zhi / Chinese Medical Association, (2002 Dec)
Vol. 5, No. 6, pp. 365-8.
Journal code: 100886162. ISSN: 1008-1275. L-ISSN: 1008-1275.
PUB. COUNTRY: China
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 21 Feb 2003
Last Updated on STN: 21 Mar 2003
Entered Medline: 20 Mar 2003

AB OBJECTIVE: To investigate the effects of Ginsenoside Rb(1) on the proliferation of Schwann cells in culture.

METHODS: Applying MTT assay and Thymidine incorporation assay, the effects of Ginsenoside Rb(1) on the proliferation of Schwann cells isolated from the sciatic nerve of adult rat were studied.

RESULTS: Ginsenoside Rb(1) (10 microg/ml) significantly induced Schwann cell proliferation, the effect was similar to NGF (50 microg/ml). At high concentrations of Ginsenoside Rb(1) (1 mg/ml), the proliferation of Schwann cells was significantly inhibited.

CONCLUSIONS: Ginsenoside Rb(1) at the optimal concentrations is found to be effective in inducing the proliferation of Schwann cells, but at higher concentrations the drug is cytotoxic for Schwann cells.

L7 ANSWER 55 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003010301 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12516657
TITLE: In vitro modulation of protective antibody responses by estrogen, progesterone and interleukin-6.
AUTHOR: Canellada Andrea; Blois Sandra; Gentile Teresa; Margni Idehu Ricardo A
CORPORATE SOURCE: Instituto de Estudios de la Inmunidad Humoral-Consejo Nacional de Investigaciones Cientificas y Tecnologicas, Universidad de Buenos Aires, Buenos Aires, Argentina. acanell8ffyb.uba.ar
SOURCE: American journal of reproductive immunology (New York, N.Y. : 1989), (2002 Nov) Vol. 48, No. 5, pp. 334-43.
Journal code: 8912860. ISSN: 1046-7408. L-ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 9 Jan 2003
Last Updated on STN: 17 Apr 2003
Entered Medline: 16 Apr 2003

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB PROBLEM: We have previously demonstrated that the addition of placental interleukin-6 (IL-6) to murine hybridomas increased asymmetric antibody synthesis. Here we analyze whether progesterone (Pg) and estrogen (E2) affect asymmetric antibody synthesis by modulating IL-6 production in hybridoma cells.

METHOD OF STUDY: Hybridoma 112D5 B cells were cultured with E2, Pg or recombinant IL-6. Cell proliferation was assessed by 3H-thymidine incorporation, and asymmetric antibodies were measured in culture supernatants by Con A fixation and enzyme-linked immunosorbent assay (ELISA). E2 and Pg-receptors (ER and PR) were evaluated in whole cell extracts by Western blot. IL-6 was measured in culture supernatants by ELISA.

RESULTS: 112D5 expressed both PR and ER, which were differentially regulated. At 48 hr, Pg and E2 slightly decreased cell proliferation whereas IL-6 did not. As well as IL-6, 10(-10) M Pg but not E2 induced asymmetric antibody production. Interestingly, Pg at 10(-6) M decreased asymmetric antibody synthesis by hybridoma cells. Finally, mainly Pg but also E2 increased IL-6 synthesis, although IL-6 levels did not correlate with asymmetric antibodies synthesized in the presence of E2 or Pg.

CONCLUSIONS: In cells expressing both ER and PR, we could demonstrate that steroids participate in humoral immune responses by modulating asymmetric antibody synthesis. IL-6 proved to be only partially involved. Other possible mechanisms involved in the effect of Pg on blocking antibody responses and their contribution to a successful pregnancy are discussed in the paper.

L7 ANSWER 56 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002460324 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12219029
TITLE: The signaling protein Rho is necessary for vascular smooth muscle migration and survival but not for proliferation.
AUTHOR: Liu Bo; Itoh Hiroyuki; Louie Otway; Kubota Kenji; Kent K Craig
CORPORATE SOURCE: Department of Surgery, Division of Vascular Surgery, Weill Medical College of Cornell University, New York Presbyterian Hospital, New York, NY 10021, USA.
CONTRACT NUMBER: 5T32GM08466 (United States NIGMS NIH HHS)
SOURCE: HL55465 (United States NHLBI NIH HHS) Surgery, (2002 Aug) Vol. 132, No. 2, pp. 317-25. Journal code: 0417347. ISSN: 0039-6060. L-ISSN: 0039-6060. United States
PUB. COUNTRY: English
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 10 Sep 2002
Last Updated on STN: 8 Oct 2002
Entered Medline: 4 Oct 2002

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB BACKGROUND: The small GTPase Rho has been implicated in a variety of cellular processes. Vascular smooth muscle cell (SMC) migration, proliferation, and apoptosis are important events that contribute to the formation of intimal hyperplasia. To better understand the importance of Rho in intimal hyperplasia, we evaluated the necessity of Rho for these 3 cellular processes.

METHODS: We used for these studies a recombinant C3 exoenzyme (C3), which selectively adenosine diphosphate-ribosylates and, thus, functionally inactivates Rho. SMC migration was determined by scratch and modified Boyden chamber assays, proliferation by tritiated-thymidine incorporation, and apoptosis by terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling.

RESULTS: Pretreatment of human SMC with C3 overnight resulted in adenosine diphosphate-ribosylation and inactivation of Rho. Inactivation of Rho completely eliminated SMC migration in response to platelet-derived growth factor (PDGF)-AB. Furthermore, C3 blocked phosphorylation of focal adhesion kinase, tensin, and paxillin, which are essential for cellular migration. In contrast, C3 did not significantly affect DNA synthesis in response to PDGF-AB or activation of mitogen-activated protein kinase, a signaling mediator of PDGF-stimulated proliferation. However, prolonged inactivation of Rho by C3 induced apoptosis of SMC.

CONCLUSIONS: The small GTPase Rho is necessary for vascular SMC migration and cell survival but not for proliferation. Manipulation of Rho might have therapeutic value in modulating intimal hyperplasia.

L7 ANSWER 57 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002443972 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12203102
TITLE: In vitro and in vivo effects of repifermin (keratinocyte growth factor-2, KGF-2) on human carcinoma cells.
AUTHOR: Alderson Ralph; Gohari-Fritsch Shiva; Olsen Hendrik; Roschke Viktor; Vance Courtney; Connolly Kevin
CORPORATE SOURCE: Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850, USA.
SOURCE: Cancer chemotherapy and pharmacology, (2002 Sep) Vol. 50, No. 3, pp. 202-12. Electronic Publication: 2002-07-30.
Journal code: 7806519. ISSN: 0344-5704. L-ISSN: 0344-5704.
PUB. COUNTRY: Germany; Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 31 Aug 2002
Last Updated on STN: 5 Jan 2003
Entered Medline: 17 Oct 2002

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
AB PURPOSE: Repifermin (keratinocyte growth factor-2, KGF-2) is a growth factor that selectively induces epithelial cell proliferation, differentiation and migration. The objective of this study was to assess the effect of repifermin on in vitro tumor cell proliferation and in vivo tumor growth using a variety of human carcinoma cell lines with differing growth rates and levels of KGF receptor (KGFR) expression.

METHODS: Potential effects of repifermin on in vitro cell proliferation were evaluated by alamarBlue and/or [(3)H]-thymidine incorporation assays under a range of serum conditions. In vivo tumor growth was evaluated by implanting KGFR(+) carcinomas subcutaneously into nude mice and measuring tumor growth over time in mice injected intravenously (i.v.) or intraperitoneally (i.p.) with repifermin or placebo.

RESULTS: In vitro, none of the 30 human carcinoma cell lines tested demonstrated a substantial increase in proliferation in response to repifermin over the concentration range 0.01 to 1000 ng/ml. In vivo results showed no significant tumor growth-promoting activity when single- or multiple-cycle intravenous injections of repifermin (1 mg/kg) were given to athymic nude mice inoculated with human KGFR(+) tumors of the pharynx (Detroit 562, FaDu), colon (Caco-2), salivary gland (A-253) or tongue (SCC-25, CAL 27). In addition, repifermin (0.2 or 2 mg/kg) injected i.p. for 2 weeks had no effect on the growth of eight other human carcinomas including those of the ovary (NIH:OVCAR-3, SK-OV 3, PA-1), bladder (ScABER), epidermis (A 431), lung (SW 900), breast (MDA-MB-231)

and cervix (SiHa).

CONCLUSIONS: Repifermin had no in vitro or in vivo proliferative effects on KGFR(+) human epithelial-like tumors. This failure to stimulate tumor cell growth highlights the ability of repifermin to specifically target normal epithelial tissue. This is critical to the safety profile of repifermin, since it is currently in phase II clinical trials for the treatment of cancer patients with mucositis resulting from chemo- or radiotherapy.

L7 ANSWER 58 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002684786 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12448768
TITLE: Influence of lithium on growth and viability of thyroid follicular cells.
AUTHOR: Gaberscek S; Kalisnik M; Pezdirc M; Pavlin K; Hojker S
CORPORATE SOURCE: Medical Centre Ljubljana, Department for Nuclear Medicine, Slovenia. simona.gaberscek@kclj.si
SOURCE: Folia biologica, (2002) Vol. 48, No. 5, pp. 200-4.
Journal code: 0234640. ISSN: 0015-5500. L-ISSN: 0015-5500.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 14 Dec 2002
Last Updated on STN: 1 May 2003
Entered Medline: 30 Apr 2003

AB Lithium accumulates in the thyroid gland and can cause goiter or thyroid dysfunction. The aims of our work were: 1) to verify whether lithium stimulates proliferation of thyroid cells; as methods, the 3H-thymidine incorporation assay and the MTT assay (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) were used; as a model system the FRTL-5 (Fischer rat thyroid cells in low serum) cell line was selected, 2) to test whether lithium can have a cytotoxic effect on FRTL-5 cells, using the cytotoxicity assay with 51Cr release and the trypan blue exclusion method. Without TSH stimulation, lithium at 0.35-2 mM concentrations significantly increased the 3H-thymidine incorporation. A similar effect was observed in the case of the MTT assay: without TSH stimulation, lithium at 0.4-2 mM concentrations showed a significant stimulation of proliferation. Surprisingly, under TSH stimulation, lithium at the 2 mM concentration significantly inhibited proliferation of FRTL-5 cells. With the cytotoxicity assay, lithium was found to increase 51Cr release at 1.4-2 mM concentrations. Additionally, the percentage of viable FRTL-5 cells at 0.35-2 mM concentrations of lithium was lower than in the controls without lithium. In conclusion, lithium was found to stimulate proliferation of FRTL-5 cells in conditions without TSH and, surprisingly, lithium in higher concentrations diminished proliferation of FRTL-5 cells under TSH stimulation. A cytotoxic effect of higher lithium concentrations was observed.

L7 ANSWER 59 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002229267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11966537
TITLE: High molecular protein of Helicobacter pylori responsible for inhibition of ornithine decarboxylase activity of human gastric cultured cells.
AUTHOR: Takashima T; Fujiwara Y; Watanabe T; Tominaga K; Oshitani N; Higuchi K; Matsumoto T; Arakawa T; Hasuma T; Yano Y; Otani S

CORPORATE SOURCE: Department of Biochemistry, Osaka City University Medical School, Abeno-ku, Osaka, Japan. d98m011@med.osaka-cu.ac.jp
SOURCE: Alimentary pharmacology & therapeutics, (2002 Apr)

Vol. 16 Suppl 2, pp. 167-73.
Journal code: 8707234. ISSN: 0269-2813. L-ISSN: 0269-2813.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 23 Apr 2002
Last Updated on STN: 16 Jul 2002
Entered Medline: 15 Jul 2002

AB BACKGROUND: Ornithine decarboxylase (ODC), a rate-limiting enzyme of polyamine biosynthesis, mediates epithelial cell proliferation and plays a critical role in the optimal repair of gastric mucosal damage. Several studies have shown that *Helicobacter pylori* inhibits the growth and proliferation of gastric cells in vitro.

AIM: To test whether *H. pylori* extract affects ODC mRNA expression and its enzyme activity in gastric cells and to examine the partial characterization of the molecule responsible for this effect.

METHODS: Human gastric cells (MKN-45) were used. Bacterial extracts from various *E. coli* or *H. pylori* strains, namely (1) *cagA*+, *vacA*+, *CagA*+, *VacA*+, (2) *cagA*+, *vacA*+, *CagA* *VacA*-; or (3) *cagA*-, *vacA*+, *CagA*-, *VacA*- were added to the cells. Cell proliferation was assessed by [³H]-thymidine incorporation, viability by MTT assay and LDH release test, ODC enzyme activity by ¹⁴CO₂ counts from L-[1-(¹⁴C)]ornithine, and ODC mRNA by Northern blotting.

RESULTS: *H. pylori* and *E. coli* extract did not affect viability of gastric cells. *H. pylori* extract, especially extracts containing a protein greater than 50 kDa, significantly inhibited proliferation and ODC activity of gastric cells while *E. coli* extract had no effect. Inhibition of ODC activity was found in extracts of all *H. pylori* strains, irrespective of *CagA* and *VacA* protein expression. Serum stimulation induces an increase in ODC mRNA while *H. pylori* extract did not affect ODC mRNA expression.

CONCLUSION: High molecular weight (greater than 50 kDa) proteins of *H. pylori* extract without *CagA* or *VacA* protein inhibited proliferation and ODC activity of human gastric cells, but did not affect ODC mRNA expression, suggesting that inhibition of ODC activity is regulated at the post-transcriptional level.

L7 ANSWER 60 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2003367273 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12901533
TITLE: The localization of adrenomedullin in rat kidney tissue and its inhibitory effect on the growth of cultured rat mesangial cells.
AUTHOR: Liu Xueguang; Zhang Zhigang; Zhang Xiurong; Zhu Hongguang; Chen Qi; Guo Muiyi
CORPORATE SOURCE: Department of Pathology, School of Basic Medical Sciences, Medical Center, Fudan University, Shanghai 200032.
SOURCE: Chinese medical sciences journal = Chung-kuo i hsueh k'o hseuh tsa chih / Chinese Academy of Medical Sciences, (2002 Sep) Vol. 17, No. 3, pp. 129-33.
Journal code: 9112559. ISSN: 1001-9294. L-ISSN: 1001-9294.
PUB. COUNTRY: China

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 7 Aug 2003
Last Updated on STN: 19 Mar 2004
Entered Medline: 18 Mar 2004

AB OBJECTIVE: To observe the localization of adrenomedullin (AM) in rat kidney tissue and its inhibitory effect on the growth of cultured rat mesangial cells (MsC).

METHODS: A monoclonal antibody against AM developed by our laboratory was used to detect the localization of AM protein in rat kidney tissue by avidin-biotin complex immunohistochemistry. The expressions of AM and its receptor CRLR mRNA on cultured glomerular epithelial cells (GEC) and MsC were investigated by Northern blot assay, and the possible effect of AM secreted by GEC on MsC proliferation was observed using [3H]thymidine incorporation as an index.

RESULTS: A specific monoclonal antibody against AM was successfully developed. AM was immunohistochemically localized mainly in glomeruli (GEC and endothelial cells), some cortical proximal tubules, medullary collecting duct cells, interstitial cells, vascular smooth muscle cells and endothelial cells. Northern blot assay showed that AM mRNA was expressed only on cultured GEC, but not on MsC, however, AM receptor CRLR mRNA was only expressed on MsC. GEC conditioned medium containing AM can inhibit MsC growth and AM receptor blocker CGRP8-37 may partially decreased this inhibitory effect.

CONCLUSION: AM produced by GEC inhibits the proliferation of MsC, which suggests that AM as an important regulator is involved in glomerular normal physiological functions and pathologic processes.

L7 ANSWER 61 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002275143 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12015027
TITLE: Development of oral DNA vaccine based on MG(7)-Ag mimotope of gastric cancer.
AUTHOR: Guo Changcun; Ding Jie; Yu Zhaocai; Han Quanli; Meng Fanning; Liu Na; Fan Daiming
CORPORATE SOURCE: PLA Institute of Digestive Diseases, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China.
SOURCE: Zhonghua zhong liu za zhi [Chinese journal of oncology], (2002 Mar) Vol. 24, No. 2, pp. 110-3.
Journal code: 7910681. ISSN: 0253-3766. L-ISSN: 0253-3766.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 17 May 2002
Last Updated on STN: 11 Sep 2002
Entered Medline: 10 Sep 2002

AB OBJECTIVE: To develop an oral DNA vaccine based on MG(7)-Ag mimotope of gastric cancer using attenuated Salmonella typhimurium and evaluate its efficacy and protective effect.

METHODS: The eukaryotic expression vector including the MG(7)-Ag mimotope and a Th epitope was constructed, and then transduced

into an attenuated *Salmonella typhimurium* to get the oral DNA vaccine. C57BL/6 J mice were orally immunized with 1×10^8 cfu *Salmonella* transfectants, with *Salmonella* harboring empty plasmid, with phosphate buffered saline (PBS) as control. At the 6th week, serum titer of MG(7) antibody was detected by ELISA. In the 8th week, a [(3)H]-thymidine incorporation assay was performed to test the proliferation of murine spleen cells to the stimulant of MG(7)-Ag mimicry peptide. At the same time, Ehrlich ascites carcinoma cells expressing MG(7)-Ag were used in tumor challenge assay to evaluate the protective effect of the immunization.

RESULTS: The oral DNA vaccine induced MG(7) antibody in mice, while in vivo unprimed proliferation assay of the spleenocytes showed no difference among the three groups. Two weeks after tumor challenge, 2 in 7 immunized mice were tumor free, while none in the control group was protected.

CONCLUSION: Oral DNA vaccine based on the MG(7)-Ag monotope is immunogenic. It is able to induce specific immunity response against tumor in mice, and the vaccine is partially protective.

L7 ANSWER 62 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002282370 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11953067
TITLE: Effect of cyclosporin A on the growth of human first trimester cytotrophoblasts in vitro.
AUTHOR: Yan Fengting; Li Dajin; Sun Xiaoxi; Zhu Ying; Wang Mingyan; Meng Yi; Yu Jiang
CORPORATE SOURCE: Laboratory of Reproductive Immunology, Institute of Obstetrics and Gynecology, Fudan University, Shanghai 200011, China.
SOURCE: Zhonghua fu chan ke za zhi, (2002 Feb) Vol. 37, No. 2, pp. 74-6.
Journal code: 16210370R. ISSN: 0529-567X. L-ISSN: 0529-567X.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 28 May 2002
Last Updated on STN: 2 Jun 2002
Entered Medline: 31 May 2002

AB OBJECTIVE: To investigate effect of cyclosporin A (CsA) on the growth of first trimester human cytotrophoblast in vitro.

METHODS: To isolate and purificate first trimester human cytotrophoblasts by way of percoll density gradient centrifugation; to evaluate the effect of CsA on in vitro proliferation of cytotrophoblasts using (3)H-thymidine incorporation assay; to analyze of cell cycle of cytotrophoblasts with flow cytometric assay; and to survey morphology of the cells by scanning electro-microscope respectively.

RESULTS: CsA could increase in vitro proliferation of first trimester human cytotrophoblasts when concentration of CsA ranged from 1×10^{-4} micromol/L to 1 micromol/L, but decrease in vitro proliferation of the cells if the concentration reached to 10 micromol/L. G(2)-M phase increased from $(2.8 \pm 0.5)\%$ to $(6.7 \pm 1.3)\%$ when the cytotrophoblasts were incubated with culture medium containing 1 micromol/L CsA for 24 hours, while S phase increased from $(14 \pm 5)\%$ to $(28 \pm 8)\%$ and apoptosis decreased from $(8.7 \pm 2.2)\%$ to $(3.6 \pm 1.0)\%$ when the culture

in the same incubating condition lasted for 48 hours. Pseudopodia of the trophoblasts increased in number and length when they were incubated in culture medium containing 1 micromol/L of CsA for 48 hours, but decreased if the concentration reached to 10 micromol/L with the same incubating duration.

CONCLUSION: CsA is able to promote growth of first trimester human cytotrophoblasts and change their morphology, which appears to increase in invasive ability.

L7 ANSWER 63 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002668484 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12428422
TITLE: [Use of photodynamic therapy for elimination of residual leukemic cells in autologous transplants of hematopoietic progenitor cells].
Využití fotodynamické terapie k odstranění reziduálních leukemických buněk z autologních transplantátů hematopoetických progenitorových buněk.
AUTHOR: Hrkal Z; Grebenova D; Cajthamlova H; Soucek J; Bartosova J; Fuchs O; Marinov I; Kobylka P; Klamova H; Sponerova D
CORPORATE SOURCE: Ústav hematologie a krevní transfuze, Praha. hrkal@uhkt.cz
SOURCE: Casopis lekaru ceskych, (2002 Sep 22) Vol. 141
Suppl, pp. 41-6.
Journal code: 0004743. ISSN: 0008-7335. L-ISSN: 0008-7335.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 14 Nov 2002
Last Updated on STN: 17 Dec 2002
Entered Medline: 3 Dec 2002
AB BACKGROUND: The increasing use of autologous hematopoietic cell support in various malignancies including leukemia and lymphoma currently bears the problem of tumor contamination of the graft with tumor cells which after re-infusion contribute to the disease relapses. It is therefore desirable to eradicate the cancer cell fraction of the graft without causing damage to the normal stem cell fraction. The purging processes based on photodynamic treatments appear to be perspective means for this purpose.
METHODS AND RESULTS: We investigated the effects of 5-aminolevulinic acid (ALA)--based photodynamic treatment (ALA-PDT) on the proliferation of human leukemia cell lines HL60 (promyelocytic leukemia), ML2 (myelomonocytic leukemia) and HEL (erythroleukemia) by 3H-thymidine incorporation into the cell DNA, on the viability of cell lines HL60, HEL, DAUDI (B-cell leukemia) and JURKAT (T-cell lymphoma) as well as of blast cells of acute myeloid leukemia (AML) patients by flow cytometry-propidium iodide assay, and on the clonogenic activities of normal human bone marrow cells by in vitro cloning assays. Under the conditions used (treatment with 1 mM ALA for 4 h at 37 degrees C followed by exposure to blue light dose of 18 J/cm2) the number of proliferating HL60 cells was reduced by 2.4 logs, of ML2 cells by 3.2 logs and of HEL cells by 1 log. From the mononuclear cell preparations of AML patients the blast cells were substantially reduced in eight out of ten patients. The clonogenic activities of normal bone marrow progenitor cells were largely spared: 52.5 +/- 8.9% of colony-forming units--granulocytes macrophages (CFU-GM), and 48.6 +/- 9.7% burst forming units--erythrocytes (BFU-E).

CONCLUSIONS: ALA-PDT appears to be usable principle for the depletion of residual leukemic cells from autologous transplants.

L7 ANSWER 64 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002310835 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12052337
TITLE: Characterization of mitogen-stimulated porcine lymphocytes using a stable fluorescent dye (PKH2) and multicolor flow cytometry.
AUTHOR: Dorn A D; Waters W R; Byers V M; Pesch B A; Wannemuehler M J
CORPORATE SOURCE: Veterinary Medical Research Institute, Iowa State University, 1802 Elwood Drive, Ames, IA 50011, USA. adorn@iastate.edu
SOURCE: Veterinary immunology and immunopathology, (2002 Aug) Vol. 87, No. 1-2, pp. 1-10.
Journal code: 8002006. ISSN: 0165-2427. L-ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 11 Jun 2002
Last Updated on STN: 2 Aug 2002
Entered Medline: 1 Aug 2002

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB Stimulation of lymphocyte proliferation using mitogens or specific antigens is a method that is used frequently to assess immune responsiveness. While useful, lymphocyte blastogenesis, or [3H]-thymidine incorporation, provides little information regarding the response of specific subsets to the stimulant. Here, we report that the fluorescent cell membrane probe, PKH2, is a useful tool for measuring the proliferation of porcine lymphocyte subpopulations by utilizing multicolor flow cytometry. For this study, mitogen-induced proliferation of porcine peripheral blood mononuclear cells (PBMCs) was measured using [3H]-thymidine incorporation as well as a flow cytometric-based proliferation assay. From the [3H]-thymidine incorporation data alone, it was observed that PBMC stimulated with either concanavalin A (Con A), phytohemagglutinin (PHA) or pokeweed mitogen (PWM) demonstrated greater proliferation on day 3 than on day 5 of culture. Using the PKH dye and flow cytometric analysis, the responsiveness of specific lymphocyte subsets to mitogen stimulation was detected. The predominant subsets of porcine lymphocytes responding to Con A or PHA stimulation were CD4(+)CD8(+), CD4(-)CD8alpha(hi), CD4(-)CD8alpha(lo) and gammadelta TCR(+) cells. PWM stimulation induced responses by CD4(+)CD8(+), CD4CD8alpha(hi) but not by CD4(-)CD8alpha(lo) or gammadelta TCR(+) cells. Con A stimulation resulted in a sustained proliferation of CD8alpha(hi) cells over the 5-day period while PHA stimulation resulted in proliferation that peaked within the first 3 days. Little or no proliferative responses were detected within the IgM(+) population (e.g. B cells). This is the first study to define the contribution of individual lymphocyte subsets to mitogen-induced proliferation of porcine PBMCs.

L7 ANSWER 65 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002068247 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11793021
TITLE: Clusterin expression during regeneration of pancreatic

islet cells in streptozotocin-induced diabetic rats.
AUTHOR: Kim B M; Han Y M; Shin Y J; Min B H; Park I S
CORPORATE SOURCE: Department of Anatomy, College of Medicine, Inha
University, Choong-Gu, Shinheung-Dong, Incheon, Korea.
SOURCE: Diabetologia, (2001 Dec) Vol. 44, No. 12, pp.
2192-202.
Journal code: 0006777. ISSN: 0012-186X. L-ISSN: 0012-186X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 22 Jan 2003
Entered Medline: 1 Apr 2002

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB AIMS/HYPOTHESIS: Beta-cell regeneration has been reported after islet
injury in an animal model for diabetes. Recently, we showed up-regulation
of clusterin after islet injury and suggested that clusterin might be
involved in cytoprotection and in the regeneration of islet cells. The
aim of this study was to investigate the correlation of clusterin
expression with islet regeneration and its effect on islet cell
replication.

METHODS: Streptozotocin was administered to rats to induce
various types of diabetes. Islet regeneration and clusterin expression
were examined after islet injuries. Clusterin cDNA was transfected to
MIN6 cells and their proliferation activity was measured by a
[3H]thymidine-incorporation assay.

RESULTS: A diabetogenic dose of streptozotocin injected in rats provoked
an immediate degeneration of beta cells. In this model, islets showed
increased clusterin expression with extensive proliferation of alpha cells
but showed poor beta-cell replication. A subdiabetogenic dose of
streptozotocin, however, led to the proliferation of beta cells with
clusterin up-regulation. In streptozotocin-treated neonatal rats,
up-regulation of clusterin was noted during beta-cell proliferation. In
all experimental models, clusterin was expressed in alpha cells in close
correlation with islet cell proliferation, higher transcription of insulin
mRNA and MAPKs activation. Cell replication was increased by 31 % in the
MIN6 cells transfected by the clusterin cDNA.

CONCLUSION/INTERPRETATION: Up-regulation of clusterin in alpha cells
might induce beta-cell proliferation and thus restore their population
after islet injury. We suggest that clusterin could be considered as a
growth factor-like molecule stimulating islet-cell proliferation by
paracrine action.

L7 ANSWER 66 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001529819 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11576351
TITLE: Ganglioside as an endogenous growth suppressor for
glomerular mesangial cells.
AUTHOR: Tsuboi N; Utsunomiya Y; Kawamura T; Kawano T; Hosoya T;
Ohno T; Yamada H
CORPORATE SOURCE: Division of Kidney and Hypertension, Department of Internal
Medicine, Institute of DNA Medicine, Jikei University
School of Medicine, Tokyo Japan. nobuotsu@aoi.com
SOURCE: Kidney international, (2001 Oct) Vol. 60, No. 4,
pp. 1378-85.
Journal code: 0323470. ISSN: 0085-2538. L-ISSN: 0085-2538.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 1 Oct 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 3 Jan 2002

AB BACKGROUND: Glomerular mesangial cells potentially secrete many growth-modulating substances that could regulate mesangial cell proliferation. To date, however, the properties of such factors have not been fully evaluated.

METHODS: For that purpose, conditioned medium (CM) from mesangial cells was used for cross-feeding experiments. Cell proliferation was evaluated by ³H-thymidine incorporation assay and direct cell counting. The growth-regulatory molecule was further characterized using biochemical techniques.

RESULTS: Cross-feeding this CM to mesangial cells in vitro, despite stimulation with platelet-derived growth factor (PDGF), effectively suppressed the cells' synthesis of DNA in a dose-dependent manner. The inhibitory substance derived from mesangial cells was less than 3 kD in molecular mass, was heat stable, and was insensitive to proteinase K. After neuraminidase digestion, this inhibitory activity was lost. These data indicated that the inhibiting substance bore the typical features of gangliosides, which are multifunctional glycolipids that reside in cell membrane. Gangliosides were abundant in the CM from mesangial cells, as detected by metabolic radiolabeling and thin-layer chromatography (TLC). This result suggested that mesangial cells constitutively shed gangliosides. The growth suppressive activity in the CM was blunted when mesangial cells were pretreated with the ganglioside synthesis inhibitor d-threo-1-phenyl-2-decanoylamino-3-morpholino-1-propanol-HCl (d-threo-PDMP; 20 micromol/L) in accordance with the decreased ganglioside content in cells. Finally, gangliosides isolated from CM of mesangial cells suppressed PDGF-induced DNA synthesis of mesangial cells.

CONCLUSIONS: These results suggest that mesangial cells constitutively shed gangliosides that then suppress the division of these cells in an autocrine-like manner.

L7 ANSWER 67 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002041977 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11769709
TITLE: Inhibition effects of octreotide on the growth of hepatocellular carcinoma in vitro and in vivo.
AUTHOR: Wang C; Tang C; Tang L
CORPORATE SOURCE: Department of Gastroenterology, First Hospital, Chongqing University of Medical Sciences, Chongqing, 400016 China.
SOURCE: Zhonghua yi xue za zhi, (2001 Oct) Vol. 81, No. 19, pp. 1194-7.
Journal code: 7511141. ISSN: 0376-2491. L-ISSN: 0376-2491.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 25 Jan 2002

Entered Medline: 15 Jan 2002

AB OBJECTIVE: To investigate the effects of somatostatin analogue octreotide on the proliferation and apoptosis of human hepatocellular carcinoma (HCC) cell line as well as the growth of HCC xenografts in nude mice.

METHODS: The effects of octreotide on the proliferation and apoptosis of SMMC-7721 HCC cells was measured by 3H-thymidine incorporation into DNA and the TdT-mediated dUTP nick end labeling assay (TUNEL) or flow cytometric assay separately. Nude mice bearing xenografts of the cell line were treated with octreotide or saline as a control daily until eight weeks after tumor implantation.

RESULTS: Incubation with octreotide decreased 3H-thymidine incorporation into DNA of SMMC-7721 cells by approximately 50% at a concentration of 1 μ mol/L. The inhibit effect of octreotide showed a concentration dependence. After 96 h incubation, total cell count was decreased 52.2% compared with control. When cells were treated by octreotide at 1 x 10⁻⁶ mol/L for 24 hours, the apoptosis rates was (15.2 +/- 2.4)%. At necropsy, in mice given octreotide, the mean tumor weight were significantly lower than that of control group (0.27 +/- 0.05 vs 0.85 +/- 0.37, P < 0.01). The inhibition rate of tumor in vivo at 2 months was 68.2%.

CONCLUSION: Octreotide is effective in inhibiting growth of HCC both in vivo and in vitro significantly. The mechanisms of antineoplastic effect action may involved in inhibiting DNA synthesize and inducing apoptosis of tumor cells.

L7 ANSWER 68 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001204303 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11159528
TITLE: Induction of cytomegalovirus (CMV)-specific T-cell responses using dendritic cells pulsed with CMV antigen: a novel culture system free of live CMV virions.
AUTHOR: Peggs K; Verfuert S; Mackinnon S
CORPORATE SOURCE: Department of Haematology, University College London, London, United Kingdom.
SOURCE: Blood, (2001 Feb 15) Vol. 97, No. 4, pp. 994-1000.
Journal code: 7603509. ISSN: 0006-4971. L-ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: (EVALUATION STUDIES)
(JOURNAL, ARTICLE; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 17 Apr 2001
Last Updated on STN: 17 Apr 2001
Entered Medline: 12 Apr 2001

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB Recipients of allogeneic transplants are at risk of cytomegalovirus (CMV) infection and disease during the period of immune compromise after transplantation. The limitations of current antiviral pharmacotherapy have led to attempts to develop alternative strategies for preventing or treating CMV infection, such as adoptive transfer of donor-derived virus-specific T cells. Methods for generating CMV-specific T cells either use live CMV to infect autologous antigen-presenting cells (APCs) or require some knowledge of the immunodominant peptides involved in the immune response. A novel culture system was developed that does not use live virions and in which the APCs are monocyte-derived dendritic cells (DCs). APCs were pulsed with CMV antigen and cocultured with

autologous peripheral blood lymphocytes from donors seropositive for CMV. The culture-output cells consisted of both CD4- and CD8-expressing T cells. Proliferation, as determined by a tritium-thymidine-incorporation assay, showed significant CMV-antigen specificity in cultures from 15 of 15 donors seropositive for CMV. In cytotoxicity assays, cytotoxic T lymphocytes from 10 of 12 cocultures specifically lysed autologous CMV-infected fibroblasts or DCs but not HLA-mismatched or uninfected target cells, and this activity was shown to be blocked by HLA class I blocking antibodies. T-cell-receptor spectratyping of cells from the cultures typically showed complex size-distribution patterns, with all size classes of a normal preculture distribution present. However, a few size-class peaks were expanded compared with the preculture patterns and these may have represented expansions of CMV-specific T-cell clones. Advantages of this culture system are that it requires no live virions and no detailed knowledge of the antigenic peptides involved and it is applicable to CMV-seropositive donors of any HLA type.

L7 ANSWER 69 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001272199 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11330966
 TITLE: The expression and action of granulocyte macrophage-colony stimulating factor and its interaction with TGF-beta in endometrial carcinoma.
 AUTHOR: Ripley D; Tang X M; Ma C; Chegini N
 CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Florida, Gainesville, FL 32610, USA.
 SOURCE: Gynecologic oncology, (2001 May) Vol. 81, No. 2, pp. 301-9.
 JOURNAL CODE: 0365304. ISSN: 0090-8258. L-ISSN: 0090-8258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200105
 ENTRY DATE: Entered STN: 29 May 2001
 Last Updated on STN: 29 May 2001
 Entered Medline: 21 May 2001
 OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
 AB OBJECTIVE: Previous studies have demonstrated that normal human endometrium expresses granulocyte macrophage-colony stimulating factor (GM-CSF) and GM-CSF receptors. Because GM-CSF is administered to cancer patients following chemotherapy, GM-CSF may directly or through interaction with ovarian steroids and other cytokines alter the behavior of endometrial cancer. The aim of this study was to determine the expression of GM-CSF and receptors in endometrial carcinoma and its direct effect and interaction with transforming growth factor beta (TGF-beta) on Ishikawa cells, a human endometrial carcinoma cell line.
 METHODS: GM-CSF, GM-CSF receptors, TGF-beta1, and TGF-beta type II receptor expression were evaluated using quantitative reverse transcription polymerase chain reaction (Q-RT-PCR). The effect of GM-CSF on DNA synthesis, cell proliferation, expression of GM-CSF, TGF-beta1, and TGF-beta receptor, and their regulation by ovarian steroids was determined by the rate of [³H]thymidine incorporation, MTT assay, Q-RT-PCR, and ELISA, respectively.
 RESULTS: Endometrial carcinomas express significantly higher GM-CSF and GM-CSF alpha and beta receptor mRNA compared with normal postmenopausal endometrium. GM-CSF at various doses had no significant effect on the rate of [³H]thymidine incorporation or proliferation of Ishikawa cells,

whereas TGF-beta1 inhibited [(3)H]thymidine incorporation. GM-CSF and TGF-beta1 regulate their own expression and the expression of TGF-beta type II receptor, which were both upregulated by 17beta-estradiol and medroxyprogesterone acetate treatment and reversed following cotreatment with their respective receptor antagonists.

CONCLUSION: Endometrial carcinoma expresses an elevated level of GM-CSF and GM-CSF receptors. GM-CSF is not a mitogen for the endometrial cancer cell line; however, either alone or through interaction with TGF-beta1, it regulates its own expression and the expression of TGF-beta1 and TGF-beta type II receptor which inhibits endometrial cancer cells. This interaction may represent a regulatory feedback mechanism that could serve to suppress endometrial carcinoma growth.

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L7 ANSWER 70 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001423643 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11471572
TITLE: Melanoma differentiation associated gene-7 (mda-7): a novel anti-tumor gene for cancer gene therapy.
AUTHOR: Mhashikar A M; Schrock R D; Hindi M; Liao J; Sieger K; Kourouma F; Zou-Yang X H; Onishi E; Takh O; Vedvick T S; Fanger G; Stewart L; Watson G J; Snary D; Fisher P B; Saeki T; Roth J A; Ramesh R; Chada S
CORPORATE SOURCE: Introgen Therapeutics Inc, Houston, TX 77030, USA.
SOURCE: Molecular medicine (Cambridge, Mass.), (2001 Apr) Vol. 7, No. 4, pp. 271-82.
Journal code: 9501023. ISSN: 1076-1551. L-ISSN: 1076-1551. Report No.: NLM-PMC1950035.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 22 Oct 2001
Last Updated on STN: 22 Oct 2001
Entered Medline: 18 Oct 2001

OS.CITING REF COUNT: 8 There are 8 MEDLINE records that cite this record
AB BACKGROUND: The mda-7 gene (melanoma differentiation associated gene-7) is a novel tumor suppressor gene. The anti-proliferative activity of MDA-7 has been previously reported. In this report, we analyze the anti-tumor efficacy of Ad-mda7 in a broad spectrum of cancer lines.

MATERIALS AND METHODS: Ad-mda7-transduced cancer or normal cell lines were assayed for cell proliferation (tritiated thymidine incorporation assay, Alamar blue assay, and trypan-blue exclusion assay), apoptosis (TUNEL, and Annexin V staining visualized by fluorescent microscopy or FACS analysis), and cell cycle regulation (Propidium Iodide staining and FACS analysis).

RESULTS: Ad-mda7 treatment of tumor cells resulted in growth inhibition and apoptosis in a temporal and dose-dependent manner. The anti-tumor effects were independent of the genomic status of p53, RB, p16, ras, bax, and caspase 3 in these cells. In addition, normal cell lines did not show inhibition of proliferation or apoptotic response to Ad-mda7. Moreover, Ad-mda7-transduced cancer cells secreted a soluble form of MDA-7 protein. Thus, Ad-mda7 may represent a novel gene-therapeutic agent for the treatment of a variety of cancers.

CONCLUSIONS: The potent and selective killing activity of Ad-mda7 in

cancer cells but not in normal cells makes this vector a potential candidate for cancer gene therapy.

L7 ANSWER 71 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002057431 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11783368
TITLE: Gene transfer of CD80 into a human ovarian cancer cell line and induction of cytotoxic T lymphocyte in vitro.
AUTHOR: Cui B; Kong B; Jiang J
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Qilu Hospital of Shandong University, Jinan 250012, China.
SOURCE: Zhonghua fu chan ke za zhi, (2001 Apr) Vol. 36, No. 4, pp. 229-32.
Journal code: 16210370R. ISSN: 0529-567X. L-ISSN: 0529-567X.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 28 Jan 2002
Entered Medline: 23 Jan 2002

AB OBJECTIVE: To investigate the proliferation and cytotoxicity of cytotoxic T lymphocyte (CTL) induced by ovarian cancer cells transfected with a CD80 gene containing retroviral vector.

METHODS: The ovarian cancer cell line TYK cells were transfected with retro-virus vector PLXSN-hCD80. After geneticin (G418) selection, the CD80 expression of the transfectants was confirmed by flow cytometry. CTL was induced by co-culture of CD80-expressing TYK cells (TYK-hCD80) and peripheral-blood mononuclear cells (PBMC) in the presence of anti-CD3 monoclonal antibody (McAb). Proliferation of PBMC was measured using 3H-Thymidine incorporation assay. The lysis activity of CTL toward tumor cells was determined using methyl thiazolyl tetrazolium (MTT) assay.

RESULTS: After transfection and G418 selection, the CD80 expression was proved by flow cytometry. The highest rate of CD80 expression was 84.9%. The TYK cell line expressing high CD80 was named TYK-hCD80. In the presence of anti-CD3 McAb, TYK-hCD80 significantly enhanced proliferation of PBMC than TYK cells (3H-Thymidine incorporation, (40,604 +/- 842) vs (8,000 +/- 594) cpm (P < 0.05). The lysis activity of CTL activated by TYK-hCD80 was higher than that of TYK(P < 0.05).

CONCLUSIONS: Ovarian cancer cells expressing CD80 can induce the production of CTLs which have high lysis activity and high proliferation rate in the presence of anti-CD3 McAb. This study may provide the experimental basis for immunogenic therapy of ovarian cancer.

L7 ANSWER 72 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001610459 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11684133
TITLE: Flow cytometric determination of cytokine production and proliferation in hepatitis B core antigen specific murine CD4 cells: lack of correlation between number of cytokine producing cells and cytokine levels in supernatant.
AUTHOR: Alheim M; Lazdina U; Milich D R; Sallberg M
CORPORATE SOURCE: Division of Clinical Virology, F 68, Karolinska Institutet at Huddinge University Hospital, SE-141 86, Huddinge, Sweden. Mats.Alheim@mpi.ki.se

SOURCE: Journal of immunological methods, (2001 Dec 1)
Vol. 258, No. 1-2, pp. 157-67.
Journal code: 1305440. ISSN: 0022-1759. L-ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 2 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 14 Dec 2001

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record

AB Hepatitis B virus (HBV) core antigen (HBcAg) has extraordinary immunostimulatory properties. The majority of studies done so far on HBcAg induced responses have used ELISA or bioassay for cytokine determination and the ³[H]thymidine incorporation assay to measure proliferation. Here multiparameter flow cytometry was used to measure HBcAg induced cytokine production and proliferation of murine T cells. The advantage with this technique was that we could analyse the cytokine phenotype of proliferating cells of a particular cell type. We found that IL-10 expression was strongly induced in CD4+ T cells after HBcAg immunization. Importantly, we found that IL-4 producing HBcAg-specific CD4+ T cells are common after immunization although detection of IL-4 in culture supernatants indicates only low levels of IL-4. In contrast, IFN-gamma producing HBcAg-specific CD4+ T cells were found at lower numbers despite the detection of high levels of IFN-gamma in culture supernatants. Thus, the frequency of these cells is not accurately reflected by the detectability of the respective cytokine in culture supernatants. A low number of specific CD4+ T cells may effectively produce high levels of cytokine. We therefore suggest that different types of cytokine assays are used in order to obtain the most accurate picture of the intrinsic cytokine phenotype of the CD4+ T cells primed by HBcAg.

L7 ANSWER 73 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001496613 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11545250
TITLE: Pro-inflammatory cytokines induce c-fos expression followed by IL-6 release in human airway smooth muscle cells.
AUTHOR: McKay S; Bromhaar M M; de Jongste J C; Hoogsteden H C; Saxena P R; Sharma H S
CORPORATE SOURCE: Department of Pharmacology, Erasmus University Medical Center, GE Rotterdam, The Netherlands.
SOURCE: Mediators of inflammation, (2001 Jun) Vol. 10, No. 3, pp. 135-42.
Journal code: 9209001. ISSN: 0962-9351. L-ISSN: 0962-9351.
Report No.: NLM-PMC1781705.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 10 Sep 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 16 Jan 2002

MEDLINE REFERENCE COUNT: 38 There are 38 cited references available in MEDLINE for this document.

AB BACKGROUND: Airway smooth muscle (ASM) is considered to be a target for mediators released during airway inflammation.

AIMS: To investigate the expression of c-fos, a constituent of the transcription factor activator protein-1, in human ASM cells. In addition, to measure the release of interleukin (IL)-6 into the conditioned medium of stimulated ASM cells, as well as DNA biosynthesis and changes in cell number.

METHODS: Serum-deprived human ASM cells in the G0/G1 phase were stimulated with the pro-inflammatory cytokines; tumour necrosis factor-alpha, IL-1beta, IL-5 and IL-6. The expression of mRNA encoding the proto-oncogene c-fos was measured by Northern blot analysis. Cell proliferation was assessed by [3H]-thymidine incorporation assays and cell counting, and IL-6 levels in cell-conditioned medium were measured by enzyme-linked immunosorbent assay.

RESULTS: All of the cytokines investigated induced a rapid (within 1 h) and transient increase in the expression of mRNA encoding c-fos, followed by the expression and enhanced release of IL-6. Cell proliferation remained unchanged in cytokine-stimulated cells.

CONCLUSIONS: Cytokine-induced c-fos expression in human ASM cells could be described as a marker of cell 'activation'. The possible association of these results with airway inflammation, through secondary intracellular mechanisms such as cytokine production, is discussed.

L7 ANSWER 74 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001204037 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11168996
TITLE: Dual effect of oxidized LDL on cell cycle in human endothelial cells through oxidative stress.
AUTHOR: Galle J; Heinloth A; Wanner C; Heermeier K
CORPORATE SOURCE: Division of Nephrology, Department of Medicine, University Hospital of Wurzburg, Wurzburg, Germany.
SOURCE: j-c.galle@mail.uni-wuerzburg.de
Kidney international. Supplement, (2001 Feb) Vol. 78, pp. S120-3.
Journal code: 7508622. ISSN: 0098-6577. L-ISSN: 0098-6577.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 17 Apr 2001
Last Updated on STN: 1 Oct 2001
Entered Medline: 12 Apr 2001
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: Oxidized low-density lipoprotein (OxLDL) exerts proliferation and apoptosis in vascular cells, depending on its concentration and the exposure time. Various steps in the cell cycle and in the apoptotic signaling cascade are modulated by O2-, and OxLDL stimulates vascular O2-formation. Here we studied the role of NADPH oxidase, a potential source for O2- formation after OxLDL stimulation, in cell proliferation, and we investigated whether OxLDL influences anti-apoptotic genes in cultured human umbilical vein endothelial cells (HUVEC). Methods and Results. OxLDL dose-dependently (10 to 300 microg/mL) stimulated O2-formation in HUVEC (detected by cytochrome c assay and by chemiluminescence of lucigenin). Low OxLDL concentrations (5 to 10 microg/mL) induced proliferation (detected by 3H-thymidine incorporation), while higher concentrations (50 to 300 microg/mL) induced apoptotic cell death (detected by Annexin

assay and DNA fragmentation). Proliferation was blocked by the antioxidants SOD and catalase and by diphenyleneiodonium (10 micromol/L), an inhibitor of the O2- generating NADPH oxidase. In addition, cells transfected with antisense oligonucleotides for NADPH oxidase showed a significantly reduced O2- formation after stimulation with OxLDL. The OxLDL effect on apoptosis was also blocked by antioxidants. Since endothelial cells are protected against apoptosis through anti-apoptotic genes, we investigated whether OxLDL overcomes protection against apoptosis through suppression of the anti-apoptotic gene A20, a zinc-finger protein. OxLDL suppressed the expression of A20 in a dose-dependent manner. CONCLUSION: These data indicate that OxLDL has a dual effect on cell cycle in HUVEC, inducing proliferation at low and apoptosis at higher concentrations. Both effects are mediated by O2- formation, with NADPH oxidase being a major source for O2-. Thus, OxLDL contributes importantly to vascular cellular turnover through the induction of oxidative stress.

L7 ANSWER 75 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001262407 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11306926
 TITLE: Sensitisation to the lipid-binding apolipoprotein allergen Der p 14 and the peptide Mag-1.
 AUTHOR: Epton M J; Dilworth R J; Smith W; Thomas W R
 CORPORATE SOURCE: TVM Telethon Institute for Child Health Research, West Perth, Australia.
 SOURCE: International archives of allergy and immunology, (2001 Jan-Mar) Vol. 124, No. 1-3, pp. 57-60.
 Journal code: 9211652. ISSN: 1018-2438. L-ISSN: 1018-2438.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200105
 ENTRY DATE: Entered STN: 21 May 2001
 Last Updated on STN: 21 May 2001
 Entered Medline: 17 May 2001
 AB BACKGROUND: The IgE-binding peptides Mag 1 and Mag 3 and the high-molecular-weight protein M-177 have been identified as parts of the apolipoprotein-like group 14 house dust mite allergen. By analogy with the homologous insect proteins, apolipoproteins are hydrophobic proteins found in lipid bodies and lipid transport particles. This explains why they degrade and are poorly represented in extracts.
 METHODS: We have examined the T cell stimulation induced by a 341-residue recombinant Der p 14 peptide equivalent to the Mag 1 polypeptide examined by others.
 RESULTS: Peripheral blood mononuclear cells from both allergic and non-allergic donors responded strongly in in vitro proliferation assays to the Der p 14 peptide to induce markedly more (3)H-thymidine incorporation than Der p 2 and the release of Th2 cytokines.
 CONCLUSIONS: The apolipoprotein-like group 14 allergens, despite their predicted hydrophobicity and lipid-binding activity, can induce high IgE responses and T cell stimulation. They appear to be important mite allergens unsuited to representation by aqueous extracts of mites.
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L7 ANSWER 76 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001367457 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11174004
 TITLE: Dilazep hydrochloride, an antiplatelet drug, inhibits lipopolysaccharide-induced mouse mesangial cell IL-6 secretion and proliferation.
 AUTHOR: Gohda T; Makita Y; Shike T; Funabiki K; Shirato I; Tomino Y
 CORPORATE SOURCE: Division of Nephrology, Department of Medicine, Juntendo University School of Medicine, Tokyo, Japan.
 SOURCE: Kidney & blood pressure research, (2001) Vol. 24, No. 1, pp. 33-8.
 Journal code: 9610505. ISSN: 1420-4096. L-ISSN: 1420-4096.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200106
 ENTRY DATE: Entered STN: 2 Jul 2001
 Last Updated on STN: 2 Jul 2001
 Entered Medline: 28 Jun 2001

AB BACKGROUND: Antiplatelet agents have been widely used to reduce proteinuria and to prevent the progression of chronic glomerulonephritis or diabetic nephropathy to end-stage renal failure. Dipyridamole, one type of antiplatelet drug, inhibits the proliferation of glomerular mesangial cells (MCs). The effect of dilazep hydrochloride (dilazep) on these cells is still obscure. The effects of dilazep on cultured MC IL-6 secretion and proliferation were investigated in the present study.

METHODS: IL-6 secretion from MC induced by bacterial lipopolysaccharide (LPS) were assessed using sandwich ELISA. LPS-induced MC proliferation was detected by 3H-thymidine incorporation and WST-1 assay (similar to MTT assay).

RESULTS: Incubation of MCs with various dosages of LPS (0, 1, 10, 50 and 100 ng/ml) induced IL-6 secretion in a dose-dependent manner. However, dilazep significantly inhibited this LPS-induced IL-6 secretion from MCs in a dose- and time-dependent manner. Dilazep also significantly inhibited MC proliferation in a dose-dependent manner.

CONCLUSION: It appears that these effects of dilazep may prevent progression of mesangial proliferative glomerulonephritis.

L7 ANSWER 77 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001379452 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11435749
 TITLE: Physiological concentrations of dopamine inhibit the proliferation and cytotoxicity of human CD4+ and CD8+ T cells in vitro: a receptor-mediated mechanism.
 AUTHOR: Saha B; Mondal A C; Majumder J; Basu S; Dasgupta P S
 CORPORATE SOURCE: Signal Transduction and Biogenic Amines Lab, Chittaranjan National Cancer Institute, Calcutta, India.
 SOURCE: Neuroimmunomodulation, (2001) Vol. 9, No. 1, pp. 23-33.
 Journal code: 9422763. ISSN: 1021-7401. L-ISSN: 1021-7401.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200109
 ENTRY DATE: Entered STN: 24 Sep 2001
 Last Updated on STN: 24 Sep 2001

Entered Medline: 20 Sep 2001

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record

AB OBJECTIVE: Dopamine, a catecholamine neurotransmitter, influences growth and proliferation of lymphocytes. Pharmacological doses of dopamine have been shown to modulate T cell functions significantly, but no information is available on the effect of physiological concentrations of circulating dopamine on CD4+ and CD8+ T cell functions. This information may be of importance since significantly elevated plasma dopamine levels were observed in humans during uncoping stress, and suppression of T cell functions during stress is a well-known phenomenon. However, the mechanism inducing the suppression of T cell functions during stress is not yet clear. In the present investigation, we evaluated the effect of the dopamine level attained in the plasma of individuals with uncoping stress on the proliferation and cytotoxicity of CD4+ and CD8+ T cells in vitro.

METHODS: T cell subpopulations were separated by panning. The effect of dopamine on IL-2-induced cell proliferation in vitro was evaluated by [3H]thymidine incorporation and cytotoxicity by 51Cr release, receptors by radioligand binding, cAMP by an assay kit and apoptosis by DNA fragmentation.

RESULTS: At these elevated physiological concentrations, dopamine was found to inhibit significantly the proliferation and cytotoxicity of CD4+ and CD8+ T cells in vitro. This dopamine-mediated inhibition of proliferation was more marked on CD8+ T cells than on CD4+ T cells. The underlying mechanism was found to be D1 class of dopamine-receptor-mediated stimulation of intracellular cAMP.

CONCLUSION: Results may be of significance to understand the role of peripheral dopamine in human neuroimmune communication in terms of physiological homeostasis in health and disease.

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L7 ANSWER 78 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2008271755 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18432816
TITLE: Measurement of human and murine interleukin 2 and interleukin 4.
AUTHOR: Davis L S; Lipsky P E; Bottomly K
CORPORATE SOURCE: University of Texas Southwestern Medical Center, Dallas, Texas, USA.
SOURCE: Current protocols in immunology / edited by John E. Coligan ... [et al.], (2001 May) Vol. Chapter 6, pp. Unit 6.3.
Journal code: 9101651. E-ISSN: 1934-368X. L-ISSN: 1934-3671.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200807
ENTRY DATE: Entered STN: 25 Apr 2008
Last Updated on STN: 16 Jul 2008
Entered Medline: 15 Jul 2008

AB This unit describes protocols employing cell lines or bioassays that can be used for the quantitation of murine total T cell growth factor (TCGF) activity, interleukin 2 (IL-2), and interleukin 4 (IL-4), and of human IL-2 and IL-4. The ability to distinguish between different growth factors is crucial to understanding the regulation of the immune response. The Basic Protocol describes the use of the CTLL-2 line to detect murine IL-2 and IL-4 in supernatants. One alternate protocol describes the

detection of IL-2 in samples of human serum or supernatants using CTLL-2 cells, while other alternate procedures describe the detection and quantitation of murine IL-4 using a mutagenized subline of CTLL-2, CT.4S, and the detection of human IL-4 using a derivative of the CT.4S mouse cell line, CT.h4S. Support protocols are provided for the quantitation of CTLL-2, CT4.S, or CT.h4S proliferation using a standard [3H] thymidine incorporation method or by using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) colorimetric assay (Support Protocol 1). Support protocols also describe the calculation of cytokine units from samples based on DNA synthesis data and procedures for the maintenance of the CTLL-2, CT.4S, and CT.h4S cell lines.

L7 ANSWER 79 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001025057 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11053304
 TITLE: Human fetal retinal pigment epithelium-induced cell cycle arrest, loss of mitochondrial membrane potential and apoptosis.
 AUTHOR: Farrokh-Siar L; Rezaei K A; Palmer E M; Patel S C; Ernest J T; van Seventer G A
 CORPORATE SOURCE: Department of Ophthalmology and Visual Science, Department of Pathology, University of Chicago, Illinois, USA. lfarrokh@midway.uchicago.edu
 SOURCE: Investigative ophthalmology & visual science, (2000 Nov) Vol. 41, No. 12, pp. 3991-8. Journal code: 7703701. ISSN: 0146-0404. L-ISSN: 0146-0404.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200011
 ENTRY DATE: Entered STN: 22 Mar 2001
 Last Updated on STN: 18 Oct 2002
 Entered Medline: 14 Nov 2000
 OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
 AB PURPOSE: To investigate the mechanism of action of the soluble immune suppressive product secreted by human fetal retinal pigment epithelial (HFRPE) cells in a model system using the human T-cell line Jurkat (Jkt).

METHODS: Pure HFRPE cells were isolated and cultured. The supernatants of both nonactivated and IFN-gamma-activated HFRPE cells were isolated. Cells from the human T-cell line Jkt were incubated either in standard culture medium or in the supernatant isolated from HFRPE cells. In the first assay Jkt cell proliferation was measured by [(3)H]thymidine incorporation. In the second assay Jkt cell apoptosis was examined for annexin V staining by flow cytometry. In the third assay Jkt cell division was evaluated with carboxyfluorescein succinimidyl ester (CFSE) fluorescent dye. In the last assay the mitochondrial transmembrane potential of Jkt cells was measured with the cationic lipophilic fluorochrome 3,3'-dihexyloxacarbocyanine iodide [DiOC(6)]. In all the assays the effect of supernatants isolated from both nonactivated and IFN-gamma-activated HFRPE cells were compared with standard culture medium. The involvement of antiapoptotic human gene bcl-x(L) was determined by using a Jkt cell line that was stably transfected with bcl-x(L).

RESULTS: The supernatant isolated from HFRPE cells significantly suppressed the cell division in Jkt cells and induced apoptosis. These effects were stronger when the supernatant was isolated from

IFN-gamma-activated HFRPE cells. The apoptosis pathway induced by the secreted product of HFRPE cells involved the early disruption of mitochondrial transmembrane potential. Although the overexpression of bcl-x(L) gene rescued the Jkt cells from supernatant-induced apoptosis, it could not restore the proliferation of Jkt cells.

CONCLUSIONS: These data suggest that HFRPE cells secrete a product that initiates an early cell cycle arrest in the human T-cell line Jkt, which is followed by the activation of an apoptotic pathway that involves the loss of mitochondrial membrane potential. The latter could be prevented by bcl-x(L) overexpression. Also these data suggest that the HFRPE-induced T-cell apoptosis may play a significant role in maintaining the immune privilege in the subretinal space.

L7 ANSWER 80 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2000348947 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10892858
TITLE: Inhibitory effect of PGE2 on EGF-induced MAP kinase activity and rabbit corneal epithelial proliferation.
AUTHOR: Kang S S; Li T; Xu D; Reinach P S; Lu L
CORPORATE SOURCE: Department of Biological Sciences, SUNY College of Optometry, New York, New York, USA.
CONTRACT NUMBER: EY04795 (United States NEI NIH HHS)
EY11653 (United States NEI NIH HHS)
SOURCE: Investigative ophthalmology
& visual science, (2000 Jul) Vol. 41, No. 8, pp. 2164-9.
Journal code: 7703701. ISSN: 0146-0404. L-ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 11 Aug 2000
Last Updated on STN: 11 Aug 2000
Entered Medline: 31 Jul 2000

OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record
AB PURPOSE: To determine in rabbit corneal epithelial cells in culture whether epidermal growth factor (EGF)-induced increases in prostaglandin (PG) E2 production inhibit both the extracellular signal-regulated kinase 2 (Erk-2), a mitogen-activated protein kinase (MAPK), cascade activation, and the mitogenic response to this growth factor.

METHODS: Serum starvation for 24 to 36 hours was used to synchronize cultures of SV40-transformed rabbit corneal epithelial (RCE) cells. The effects of exogenous PGE2, inhibition of PGE2 synthesis, and modulation of protein kinase A (PKA) activity on EGF-induced Erk-2 activation were assessed by immunoprecipitation, kinase assays, and Western blot analysis. PGE2 synthesis was measured by using enzyme-linked immunosorbent assay. [3H]-Thymidine incorporation was used to measure RCE cell proliferation rates.

RESULTS: EGF (5 ng/ml) significantly increased PGE2 production in a time-dependent manner up to 94%+/-8% after 3 hours. EGF-induced PGE2 production was suppressed by AACOCF3, a phospholipase A2 (cPLA2) inhibitor. EGF-induced Erk-2 activation reached a maximal level at 15 minutes, followed by a decline toward the control level after 3 hours. In the presence of either PGE2 (50 microg/ml) or 8-CPT-cAMP (100 microM), the EGF-induced Erk-2 activation was lessened. PKA was activated by applications of EGF or PGE2 and suppressed by AACOCF3. On the other hand,

either inhibition of PGE2 production with AACOCF3 or H-89, a PKA inhibitor, enhanced EGF-induced Erk-2 activity. Raf-1 activity was stimulated by EGF to maximal activity at 5 minutes and returned toward its control level after 60 minutes. As with the dependence of Erk-2 activity on PKA activity, in the presence of H-89, the EGF-induced Raf-1 activation was significantly enhanced. DNA synthesis was increased 59% \pm 5% (n = 4) after EGF stimulation, indicating a mitogenic effect of EGF in RCE cells. Inhibition of cPLA2 activity with AACOCF3 increased DNA synthesis in RCE cells by another 64% relative to the effect of EGF alone. In contrast, with either PGE2 or 8-CPT-cAMP present the mitogenic response to EGF was totally suppressed.

CONCLUSIONS: EGF-induced increases in PGE2 production dampened the mitogenic response to this growth factor. This suppression appears to be a consequence of PGE2-elicited increases in PKA activity, which leads to inhibition of EGF-induced activation of MAPK cascades at the level of Raf-1 and further affects downstream events including Erk-2. These results indicate that the mitogenic response to EGF in vivo in the proliferating basal cell layer may be dependent on the level of its PKA activity.

L7 ANSWER 81 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2000191042 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10728698
 TITLE: Identification of a human glioma-associated growth factor gene, granulin, using differential immuno-absorption.
 AUTHOR: Llau L M; Lallone R L; Seitz R S; Buznikov A; Gregg J P; Kornblum H I; Nelson S F; Bronstein J M
 CORPORATE SOURCE: Division of Neurosurgery, Jonsson Comprehensive Cancer Center, University of California at Los Angeles School of Medicine, 90095-6901, USA. lllau@mednet.ucla.edu
 CONTRACT NUMBER: CA82666-01 (United States NCI NIH HHS)
 SOURCE: Cancer research, (2000 Mar 1) Vol. 60, No. 5, pp. 1353-60.
 Journal code: 2984705R. ISSN: 0008-5472. L-ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200004
 ENTRY DATE: Entered STN: 21 Apr 2000
 Last Updated on STN: 21 Apr 2000
 Entered Medline: 11 Apr 2000
 OS.CITING REF COUNT: 12 There are 12 MEDLINE records that cite this record
 AB Identification of the genes that are differentially expressed in brain tumor cells but not in normal brain cells is important for understanding the molecular basis of these neurological cancers and for defining possible targets for therapeutic intervention. In an effort to discover potentially antigenic proteins that may be involved in the malignant transformation and progression of human glioblastomas, a novel antibody-based approach was developed to identify and isolate gene products that are expressed in brain tumors versus normal brain tissue. Using this method, whereby tumor-specific antibodies were isolated and used to screen a glioblastoma cDNA expression library, 28 gene products were identified. Nine of these clones had homology to known gene products, and 19 were novel. The expression of these genes in multiple different human gliomas was then evaluated by cDNA microarray hybridization. One of the isolated clones had consistently higher levels of expression (3-30-fold) in brain tumors compared with normal brain. Northern blot analysis and in situ hybridization confirmed this

differential overexpression. cDNA sequence analysis revealed that this gene was identical to a relatively new class of growth regulators known as granulins, which have tertiary structures resembling the epidermal growth factor-like proteins. The 2.1-kb granulin mRNA was expressed predominantly in glial tumors, with lower levels in spleen, kidney, and testes, whereas expression was not detected in non-tumor brain tissues. Functional assays using [3H]thymidine incorporation indicated that granulin may be a glial mitogen, as addition of synthetic granulin peptide to primary rat astrocytes and three different early-passage human glioblastoma cultures increased cell proliferation in vitro, whereas increasing concentrations of granulin antibody inhibited cell growth in a dose-dependent manner. The differential expression pattern, tissue distribution, and implication of this glioma-associated molecule in growth regulation suggest a potentially important role for granulin in the pathogenesis and/or malignant progression of primary brain neoplasms.

L7 ANSWER 82 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001231750 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11093284
 TITLE: Fetal pancreatic islets express functional leptin receptors and leptin stimulates proliferation of fetal islet cells.
 AUTHOR: Islam M S; Sjöholm A; Emilsson V
 CORPORATE SOURCE: Rolf Luft Center for Diabetes Research, Department of Molecular Medicine, Karolinska Institutet, Karolinska Hospital, Stockholm, Sweden. Shahidul.Islam@molmed.ki.se
 SOURCE: International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity, (2000 Oct) Vol. 24, No. 10, pp. 1246-53.
 Journal code: 9313169. ISSN: 0307-0565. L-ISSN: 0307-0565.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200105
 ENTRY DATE: Entered STN: 17 May 2001
 Last Updated on STN: 17 May 2001
 Entered Medline: 3 May 2001
 OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
 AB OBJECTIVE: Previous studies have demonstrated that leptin can stimulate proliferation of insulin-secreting tumor cell lines. The objective of this study was to characterize whether leptin could stimulate proliferation of primary beta-cells too. Since adult beta-cells have very limited capacity for replication, we examined the effect of leptin on islets of Langerhans obtained from fetal rats, in a tissue culture system.
 METHODS: Leptin receptor mRNA and c-fos mRNA were measured by RT-PCR. Proliferation of fetal rat islet cells was measured by a WST-1 colorimetric assay and [3H]-thymidine incorporation assay.

RESULTS: Leptin stimulated proliferation of serum-deprived fetal rat islet cells, as indicated by increased formation of formazan dye from a tetrazolium salt WST-1. Leptin stimulated DNA synthesis in islet cells, as indicated by increased [3H]-thymidine incorporation into DNA. The effect of leptin on islet cell proliferation was on average 39-50% of the effect obtained with 10% fetal bovine serum. Leptin increased c-fos mRNA expression by 2.8-fold in isolated fetal islets after 30 min treatment. In fetal pancreatic islets, both the common extracellular portion (OB-R) and the intact long form (OB-Rb) of the leptin receptor were readily

detected by reverse transcriptase polymerase chain reaction.

CONCLUSION: Functional leptin receptors are expressed in pancreatic islet cells, as early as during the fetal stage of development of these microorgans. Leptin stimulates proliferation of fetal islet cells and might play a role in determining islet cell mass at birth.

L7 ANSWER 83 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2000500262 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11045640
TITLE: Pharmacodynamics of mycophenolic acid in heart allograft recipients: correlation of lymphocyte proliferation and activation with pharmacokinetics and graft histology.
AUTHOR: Gummert J F; Barten M J; van Gelder T; Billingham M E; Morris R E
CORPORATE SOURCE: Transplantation Immunology, Department of Cardiothoracic Surgery, Stanford University Medical School, CA 94305-5407, USA.
SOURCE: Transplantation, (2000 Oct 15) Vol. 70, No. 7, pp. 1038-49.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 7 Nov 2000

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record

AB BACKGROUND: Assays of drug blood levels are used for therapeutic immunosuppressive drug monitoring (pharmacokinetics, PK). We monitored lymphocyte functions (pharmacodynamics, PD) in allograft recipients treated with mycophenolic acid (MPA) to determine its mechanisms and the relationships among dose levels, PK, PD, and histological severity of graft rejection.

METHODS: Lewis rats transplanted with Brown Norway (BN) rat hearts were treated with different dose levels of MPA for 8, 15, or 29 days at which times grafts were removed and scored for rejection grade. Blood was analyzed (high-performance liquid chromatography) for MPA plasma concentrations (area under the concentration-time curve 0-24 hr, C6 hr, trough) and for lymphocyte functions using concanavalin A-stimulated whole blood assays to measure lymphocyte proliferation (tritium labeled thymidine incorporation and flow cytometric bivariate proliferating nuclear cell antigen/DNA analysis) and activation (percent lymphocytes expressing CD25 or CD134). PD values were AUE0-24 hr (area under the PD effect-time curve), maximum inhibition and trough.

RESULTS: MPA equipotently suppressed (by flow cytometry) both proliferation and activation and these effects correlated with MPA plasma levels ($r^2=0.80-0.91$). Relationships among MPA dose levels, PK and PD were clear, direct, and reproducible. Correlation coefficients after 8 days of MPA treatment were: 0.90, 0.87, and 0.49 for MPA PK (AUC0-24 hr, C6 hr and trough) versus rejection scores; 0.80-0.89, 0.86-0.92, and 0.25-0.52 for PD flow cytometric assays (AUE0-24 hr, maximum inhibition, and trough) versus rejection scores.

CONCLUSIONS: MPA inhibits both lymphocyte proliferation and activation. PD by flow cytometry (FCM) correlates highly with severity of graft

rejection, showing that PD of MPA measured in peripheral blood predicts immune cell activity in graft tissue.

L7 ANSWER 84 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2002006956 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11236636
TITLE: Regulatory effect of antisense VEGF121 cDNA transfection on angiogenesis and metastasis of human lung giant cell carcinoma.
AUTHOR: Wu X; Zheng J; Fu J
CORPORATE SOURCE: Department of Pathology, Peking University, Beijing 100083, China.
SOURCE: Zhonghua yi xue za zhi, (2000 Dec) Vol. 80, No. 12, pp. 943-6.
Journal code: 7511141. ISSN: 0376-2491. L-ISSN: 0376-2491.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
(IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 21 Jan 2002
Last Updated on STN: 2 Oct 2002
Entered Medline: 1 Oct 2002

AB OBJECTIVE: To study the regulatory effect of antisense VEGF121 cDNA transfection on endogenous VEGF secretion and angiogenesis of human metastatic lung carcinoma cell line PG and explore the significance of microvessel density (MVD) in tumor growth and metastasis.

METHODS: The eukaryotic expression vectors bearing antisense VEGF121 cDNA was transfected into PG cells. Human umbilical vein endothelial cells (HUVEC) were cultured in conditioned mediums from transfected cells, and proliferation was determined by methyl thiazolyl tetrazolium (MTT) and 3H thymidine incorporation (3H TdR) assays in vitro. Microvessel density (MVD) in xenografted tumors in nude mice was analyzed by immunohistochemistry.

RESULTS: The transfectant of antisense VEGF121 cDNA exhibited a reduction in VEGF secretion. HUVEC grown in conditioned medium from the antisense VEGF transfected cells exhibited a decrease in capacities of DNA syntheses and cell proliferation. MVD of tumor with transfected antisense VEGF gene was significantly lower than that in control vector.

CONCLUSION: Antisense VEGF gene transfection can inhibit vascular endothelial cell proliferation in vitro and tumor angiogenesis in vivo, which may explain its inhibitory effects on tumor growth and metastasis.

L7 ANSWER 85 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2000266228 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10805884
TITLE: Mitogenicity and release of vascular endothelial growth factor with and without heparin from fibrin glue.
AUTHOR: Shireman P K; Greisler H P
CORPORATE SOURCE: Division of Peripheral Vascular Surgery, Department of Surgery, Loyola University Medical Center, Hines V. A. Hospital, Maywood, Ill, USA.
CONTRACT NUMBER: R01 HL41272 (United States NHLBI NIH HHS)
SOURCE: Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society

for Cardiovascular Surgery, North American Chapter,
(2000 May) Vol. 31, No. 5, pp. 936-43.
Journal code: 8407742. ISSN: 0741-5214. L-ISSN: 0741-5214.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20 Jul 2000
Last Updated on STN: 20 Jul 2000
Entered Medline: 7 Jul 2000

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB PURPOSE: Fibrin glue (FG) has been used for local cytokine delivery on both vascular grafts and angioplasty sites. We measured the diffusive release of vascular endothelial growth factor (VEGF) and heparin from FG and the mitogenic activity of VEGF with and without heparin in FG on canine endothelial cells (ECs) and smooth muscle cells (SMCs).

METHODS: Release of VEGF labeled with iodine 125 and tritiated heparin from FG into the overlying media was serially measured over 96 hours, and the data are reported as the mean percent released +/- SD. Proliferation assays measuring tritiated thymidine incorporation were performed for ECs and SMCs plated in media with 10% serum on FG containing various concentrations of VEGF and heparin. Media was placed on the FG for 24 hours and removed before plating cells to minimize the effect of the released, soluble VEGF and heparin.

RESULTS: At 24 hours, 54% +/- 1% and 58% +/- 1% of the radioactive VEGF and heparin were released, respectively, with minimal release thereafter (58% +/- 1% and 66% +/- 1% at 96 hours). The ECs, SMCs, or media only (no cells) was plated on FG containing radioactive VEGF in an immediate or 24-hour delayed fashion for 72 hours to determine the percent release of VEGF into the media with the two different methods of plating. Cell type and the presence or absence of cells did not affect VEGF release, but there was three times more VEGF in the media for the immediate versus delayed plating (P <.001). Without heparin, VEGF at 100 ng/mL or more in the FG was needed to induce EC proliferation. Heparin at 5 U/mL enhanced EC proliferation at the VEGF dose of 100 ng/mL as compared with no heparin (P <.001), but not at the VEGF dose of 1000 ng/mL, which likely represents a maximal response. With heparin at 500 U/mL, the ECs died. In contrast, VEGF, in the presence or absence of heparin, did not affect SMC proliferation.

CONCLUSIONS: We conclude that FG with VEGF at 1000 ng/mL and heparin at 5 U/mL is the optimal concentration for in vivo use because this may encourage EC, but not SMC, proliferation. The VEGF at 1000 ng/mL should leave mitogenic concentrations of VEGF intact after the initial, diffusive loss, and the addition of heparin at 5 U/mL may enhance VEGF mitogenic activity.

L7 ANSWER 86 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001455859 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11501167
TITLE: Inhibitory effects of purified green tea epicatechins on contraction and proliferation of arterial smooth muscle cells.
AUTHOR: Chen Z Y; Law W I; Yao X Q; Lau C W; Ho W K; Huang Y
CORPORATE SOURCE: Departments of Biochemistry and Department of Physiology, Faculty of Medicine, Chinese University of Hong Kong,

SOURCE: Shatin, Hong Kong, China.
Acta pharmacologica Sinica, (2000 Sep) Vol. 21,
No. 9, pp. 835-40.
Journal code: 100956087. ISSN: 1671-4083. L-ISSN:
1671-4083.

PUB. COUNTRY: China
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 15 Aug 2001
Last Updated on STN: 30 Oct 2002
Entered Medline: 18 Oct 2001

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record

AB AIM: The present study was aimed to examine the vasorelaxant and
antiproliferative responses to purified green tea epicatechin mixture,
(-)epicatechin and (-)epigallocatechin gallate on rat arterial smooth
muscle cells.

METHODS: Changes in isometric force were measured by Grass
force transducer and effects on cell proliferation were
evaluated using [3H]thymidine incorporation
assay.

RESULTS: Epicatechin mixture, (-)epicatechin and (-)epigallocatechin
gallate, which we isolated and purified from jasmine green tea,
concentration-dependently, reduced the contractile response to
phenylephrine in rat isolated aortic rings with (-)epigallocatechin
gallate being more effective. These three agents also inhibited
[3H]thymidine incorporation into DNA in cultured rat aortic smooth muscle
cells in a concentration-dependent manner.

CONCLUSION: The purified epicatechin derivatives from jasmine green tea
relaxed the isolated rat arteries precontracted by phenylephrine and
inhibited aortic smooth muscle cell proliferation.

L7 ANSWER 87 OF 188 MEDLINE on STN

ACCESSION NUMBER: 2000425599 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10882673

TITLE: Nonradioactive techniques for measurement of in vitro
T-cell proliferation: alternatives to the [(3)H]
thymidine incorporation assay.

AUTHOR: Messele T; Roos M T; Hamann D; Koot M; Fontanet A L;
Miedema F; Schellekens P T; Rinke de Wit T F

CORPORATE SOURCE: Ethiopian-Netherlands AIDS Research Project at the
Ethiopian Health and Nutrition Research Institute, Addis
Ababa, Ethiopia. enarp@telecom.net.et

SOURCE: Clinical and diagnostic laboratory immunology, (2000
Jul) Vol. 7, No. 4, pp. 687-92.
Journal code: 9421292. ISSN: 1071-412X. L-ISSN: 1071-412X.
Report No.: NLM-PMC95935.

PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 22 Sep 2000
Last Updated on STN: 18 Dec 2002

Entered Medline: 12 Sep 2000

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
MEDLINE REFERENCE COUNT: 33 There are 33 cited references available in
MEDLINE for this document.

AB T-cell proliferation is an important in vitro parameter of in vivo immune function and has been used as a prognostic marker of human immunodeficiency virus type 1 (HIV-1) disease progression. The proliferative capacity of T cells in response to various stimuli is commonly determined by a radioactive assay based on incorporation of [³H]thymidine ([³H]TdR) into newly generated DNA. In order to assess techniques for application in laboratories where radioactive facilities are not present, two alternative methods were tested and compared to the [³H]TdR assay as a "gold standard." As an alternative, T-cell proliferation was measured by flow cytometric assessment of CD38 expression on T cells and by an enzyme-linked immunosorbent assay (ELISA) based on bromo-2'-deoxyuridine (BrdU) incorporation. Peripheral blood mononuclear cells (PBMCs), either in whole blood or Ficoll-Isopaque separated, from a total of 26 HIV-1-positive and 18 HIV-1-negative Dutch individuals were stimulated with CD3 monoclonal antibody (MAb) alone, a combination of CD3 and CD28 MAbs, or phytohemagglutinin. BrdU incorporation after 3 days of stimulation with a combination of CD3 and CD28 MAbs correlated excellently with the [³H]TdR incorporation in both study groups (HIV-1 positives, $r = 0.96$; HIV-1 negatives, $r = 0.83$). A significant correlation of absolute numbers of T cells expressing CD38 with [³H]TdR incorporation, both in HIV-1-positive ($r = 0.96$) and HIV-1-negative ($r = 0.84$) individuals, was also observed under these conditions. The results of this study indicate that determination of both the number of CD38-positive T cells and BrdU incorporation can be used as alternative techniques to measure the in vitro T-cell proliferative capacity. The measurement of CD38 expression on T cells provides the additional possibility to further characterize the proliferating T-cell subsets for expression of other surface markers.

L7 ANSWER 88 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001355328 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11324428
TITLE: Effects of XW630 on cell proliferation, iNOS activity, and cGMP content in human osteoblast-like cell line TE85.
AUTHOR: Sun L; Weng L L; Zheng H; Liu J S
CORPORATE SOURCE: Department of Pharmacology, Institute of Basic Medical Sciences, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100005, China.
SOURCE: Acta pharmacologica Sinica, (2000 Mar) Vol. 21, No. 3, pp. 261-4.
Journal code: 100956087. ISSN: 1671-4083. L-ISSN: 1671-4083.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 25 Jun 2001
Last Updated on STN: 30 Oct 2002
Entered Medline: 21 Jun 2001
AB AIM: To study the effects of 2-[3-estrone-N-ethyl-piperazine-methyl] tetracycline (XW630) in human osteoblast-like cell line TE85.

METHODS: [³H]Thymidine incorporation and cell count for cell proliferation, radioimmunoassay for cyclic GMP (cGMP) content, and monitoring the conversion of [³H]arginine for inducible nitric-oxide synthase (iNOS) activity assay.

RESULTS: After treatment with XW630 for 48 h, [3H]thymidine incorporation and cell numbers increased by 62.7% and 96.9%, respectively. NG-monomethyl-L-arginine (L-NMMA, an NOS inhibitor) induced a concentration-dependent inhibitory effect on the proliferation after treatment for 48 h. The inhibitory effect was prevented partially by XW630 (1.0 nmol.L⁻¹). After treatment with XW630 for 12-48 h, iNOS activity and cGMP concentration increased in time-dependent manners.

CONCLUSION: XW630 stimulated cell proliferation, enhanced iNOS activity and cGMP content in human osteoblast-like cell line TE85.

L7 ANSWER 89 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2001041160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11074661
TITLE: Retinoic acid receptor status in mouse spleen during a primary immune response against beta-galactosidase.
AUTHOR: Brtko J; Hartl A; Weiss R; Scheibhofer S; Mostboeck S; Thalhammer J
CORPORATE SOURCE: Institute of Experimental Endocrinology, Slovak Academy of Sciences, 833 06 Bratislava, Slovakia.
SOURCE: Endocrine regulations, (2000 Sep) Vol. 34, No. 3, pp. 113-8.
PUB. COUNTRY: Slovakia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 7 Dec 2000
AB OBJECTIVE: Evaluation of the dynamics of all-trans retinoic acid receptor binding properties in mouse spleen nuclear extracts during a primary immune response against beta-galactosidase.

METHODS: Female BALB/c mice, aged between 5 and 6 weeks were immunized intradermally into the shaved back (4 spots each) with 100 microg beta-galactosidase in 100 microl sterile phosphate buffered saline (pH 7.2) and blood was taken by tail bleeding on days 0 (preimmune serum), 4 and 6. Production of antibody in serum and the detection of cytokines (IL-4, IFN-gamma) from proliferation supernatants were determined by ELISA. Antigen-specific proliferation assay of isolated spleen cells was based on [3H]-thymidine incorporation measured in a liquid scintillation counter. Both, the maximal binding capacity (Bmax) and the affinity (Ka) of all-trans retinoic acid nuclear receptors (RAR) were evaluated according to Brtko (1994).

RESULTS AND CONCLUSIONS: Injection of beta-galactosidase induced the first detectable antibody responses on day 4 (IgM) and on day 6 (IgG). These points of time, reflecting the early and the mature immune response served to measure the antigen-specific proliferation and production of IL-4 and IFN-gamma in the supernatants of the proliferation cultures as well as all-trans retinoic acid receptor (RAR) binding characteristics in spleen nuclear proteins. The RAR Bmax was significantly (P<0.05) decreased only at the time of the first specific IgG antibody production.

CONCLUSIONS: The data obtained indicate the involvement of RAR in the late phase of an in vivo immune response.

L7 ANSWER 90 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2000392714 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10859486
 TITLE: Modulation of early immune responses and suppression of Trypanosoma brucei brucei infections by surgical denervation of the spleen.
 AUTHOR: Liu Y; Mustafa M; Li H L; Nuortio L; Mustafa A; Bakhtiet M
 CORPORATE SOURCE: Department of Infectious Diseases, Karolinska Institute, Huddinge University Hospital, Stockholm, Sweden.
 SOURCE: Neuroimmunomodulation, (2000) Vol. 8, No. 1, pp. 31-8.
 Journal code: 9422763. ISSN: 1021-7401. L-ISSN: 1021-7401.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200008
 ENTRY DATE: Entered STN: 24 Aug 2000
 Last Updated on STN: 24 Aug 2000
 Entered Medline: 17 Aug 2000
 AB OBJECTIVE: To examine critical interactions between the nervous system and the immune system during experimental African trypanosomiasis.

METHODS AND RESULTS: Inoculation of Trypanosoma brucei brucei resulted in early interferon (IFN)-gamma production, elevated corticosterone and prostaglandin E(2) (PGE(2)) levels and increased splenocyte proliferation, as measured by enzyme-linked immunospot assay, radioimmunoassay and thymidine incorporation assay, respectively. Splenic denervation suppressed IFN-gamma, corticosterone and PGE(2) production, enhanced splenocyte proliferation, and significantly reduced parasitemia and prolonged rat survival.

CONCLUSIONS: Our data show substantial effects of the nervous system on early immune responses that may influence the outcome of this disease. These effects were not dependent on cytokine inhibitory mediators such as prostaglandins or stress hormones. More investigations are required to understand the evident neural control over the immune system during infectious challenges, which may assist in novel therapeutic approaches.
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L7 ANSWER 91 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 2001048660 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10934619
 TITLE: Transforming growth factor beta one (TGF-beta 1) enhancement of the chondrocytic phenotype in aged perichondrial cells: an in vitro study.
 AUTHOR: Lee M C; Goomer R S; Takahashi K; Harwood F L; Amiel M; Amiel D
 CORPORATE SOURCE: Department of Orthopaedics, Connective Tissue Biochemistry, University of California, San Diego, La Jolla, USA.
 CONTRACT NUMBER: AG07996 (United States NIA NIH HHS)
 AR28467 (United States NIAMS NIH HHS)
 SOURCE: The Iowa orthopaedic journal, (2000) Vol. 20, pp. 11-6.
 Journal code: 8908272. ISSN: 1541-5457. L-ISSN: 1541-5457.
 Report No.: NLM-PMC1888754.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001

Last Updated on STN: 22 Mar 2001
Entered Medline: 14 Dec 2000

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
MEDLINE REFERENCE COUNT: 25 There are 25 cited references available in MEDLINE for this document.

AB BACKGROUND: Perichondrium is recognized as a tissue with chondrogenic potential yielding cells which can be used for osteochondral repair. Factors which influence the proliferative ability and chondrocytic phenotype of such cells include age and presence of specific growth factors, i.e. TGF-beta 1. The present in vitro study assessed proliferation and markers of chondrocytic phenotype in cells extracted from the rib perichondrium of four- to five-year-old aged rabbits, and assessed the effects of exogenously added TGF-beta 1 on those cells.

METHODS: Assays included 3H-thymidine incorporation (cell proliferation), 35S-sulfate incorporation (proteoglycan synthesis) and quantitative RT-PCR for determination of type II collagen gene expression.

RESULTS: The results demonstrated that addition of TGF-beta 1 to the culture media stimulated thymidine incorporation and proteoglycan synthesis up to four- and five-fold, respectively, in aged perichondrium-derived cells. Moreover, the exogenous addition of TGF-beta 1 to the culture media resulted in an upregulation of transcriptional expression of the type II collagen gene.

CONCLUSIONS: In summary, the present study has demonstrated that exogenously added TGF-beta 1 can stimulate proliferation and chondrocytic phenotype in aged perichondrium-derived cells in vitro.

L7 ANSWER 92 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1999282994 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10354272
TITLE: Thrombospondin peptides are potent inhibitors of mesangial and glomerular endothelial cell proliferation in vitro and in vivo.
AUTHOR: Hugo C P; Pichler R P; Schulze-Lohoff E; Prols F; Adler S; Krutsch H C; Murphy-Ullrich J E; Couser W G; Roberts D D; Johnson R J
CORPORATE SOURCE: Division of Nephrology, Universitat Erlangen-Nurnberg, Erlangen, Germany. mfm444@remail.uni-erlangen.de
CONTRACT NUMBER: DK-02142 (United States NIDDK NIH HHS)
DK-43422 (United States NIDDK NIH HHS)
HL-18645 (United States NHLBI NIH HHS)
SOURCE: Kidney international, (1999 Jun) Vol. 55, No. 6, pp. 2236-49.
Journal code: 0323470. ISSN: 0085-2538. L-ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999

Entered Medline: 6 Jul 1999

AB BACKGROUND: Thrombospondin 1 (TSP1), a multifunctional, matricellular glycoprotein, is expressed de novo in many inflammatory disease processes, including glomerular disease. Short peptide fragments derived from the type I propeptide repeats of the TSP1 molecule mimic anti-angiogenic and/or transforming growth factor-beta (TGF-beta)-activating properties of the whole TSP1 glycoprotein. We investigated the effects of D-reverse peptides derived from the type I domain of TSP1 in experimental mesangial proliferative glomerulonephritis in the rat (anti-Thyl model), as well as their effects on cultured mesangial and glomerular endothelial cells.

METHODS: Effects of TSP peptides on proliferation of mesangial or glomerular endothelial cells in culture after growth arrest or growth factor stimulation (fibroblast growth factor-2, platelet-derived growth factor-BB, 10% fetal calf serum) were measured by [3H] thymidine incorporation assay. Adhesion of rat mesangial cells (MCs) to a TSP-peptide matrix was assayed using an attachment-hexosaminidase assay. TSP peptides were intraperitoneally injected daily in rats that had received an intravenous injection of polyclonal anti-Thyl antibody to induce mesangial proliferative glomerulonephritis. On biopsies from days 2, 5, and 8 of anti-Thyl disease, mesangial and glomerular endothelial proliferation, matrix expansion, mesangial activation, and microaneurysm formation were assessed. Functional parameters such as blood pressure and proteinuria were also measured.

RESULTS: An 18-amino acid peptide (type I peptide) with anti-angiogenic and TGF-beta-activating sequences decreased mesangial and glomerular endothelial cell proliferation in vitro and in vivo and reduced microaneurysm formation and proteinuria in experimental glomerulonephritis. Analogues lacking the TGF-beta-activating sequence mimicked most effects of the type I peptide. The mechanism of action of these peptides may include antagonism of fibroblast growth factor-2 and alteration of MC adhesion. The TGF-beta-activating sequence alone did not have significant effects on mesangial or glomerular endothelial cells in vitro or in experimental kidney disease in vivo.

CONCLUSION: Peptides from TSP1 may be promising therapeutics in treating glomerular disease with mesangial and endothelial cell injury.

L7 ANSWER 93 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1999221691 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10205210
TITLE: Vicia faba agglutinin, the lectin present in broad beans, stimulates differentiation of undifferentiated colon cancer cells.
AUTHOR: Jordinson M; El-Hariry I; Calnan D; Calam J; Pignatelli M
CORPORATE SOURCE: Division of Investigative Science, Imperial College of Science, Technology, and Medicine, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK.
CONTRACT NUMBER: (United Kingdom Wellcome Trust)
SOURCE: Gut, (1999 May) Vol. 44, No. 5, pp. 709-14.
Journal code: 2985108R. ISSN: 0017-5749. L-ISSN: 0017-5749.
Report No.: NLM-PMC1727505.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 18 Jun 1999
Last Updated on STN: 18 Dec 2002

Entered Medline: 10 Jun 1999

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
MEDLINE REFERENCE COUNT: 32 There are 32 cited references available in
MEDLINE for this document.

AB BACKGROUND: Dietary lectins can alter the proliferation of colonic cells.
Differentiation is regulated by adhesion molecules which, being
glycosylated, are targets for lectin binding.

AIMS: To examine the effects of dietary lectins on differentiation,
adhesion, and proliferation of colorectal cancer cells.

METHODS: Differentiation was assessed in three dimensional
gels, adhesion by aggregation assay, and proliferation
by 3H thymidine incorporation. The role of the
epithelial cell adhesion molecule (epCAM) was studied using a specific
monoclonal antibody in blocking studies and Western blots. The human
colon cancer cell lines LS174T, SW1222, and HT29 were studied.

RESULTS: The cell line LS174T differentiated in the presence of Vicia
faba agglutinin (VFA) into gland like structures. This was inhibited by
anti-epCAM monoclonal antibody. Expression of epCAM itself was
unaffected. VFA as well as wheat germ agglutinin (WGA) and the edible
mushroom lectin (Agaricus bisporus lectin, ABL) significantly aggregated
LS174T cells but peanut agglutinin (PNA) and soybean agglutinin (SBA) did
not. All lectins aggregated SW1222 and HT29 cells. Aggregation was
blocked by the corresponding sugars. Aggregation of cells by VFA was also
inhibited by anti-epCAM. VFA, ABL, and WGL inhibited proliferation of all
the cell lines; PNA stimulated proliferation of HT29 and SW1222 cells. In
competition studies all sugars blocked aggregation and proliferation of
all cell lines, except that the addition of mannose alone inhibited
proliferation.

CONCLUSION: VFA stimulated an undifferentiated colon cancer cell line to
differentiate into gland like structures. The adhesion molecule epCAM is
involved in this. Dietary or therapeutic VFA may slow progression of
colon cancer.

L7 ANSWER 94 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1999221682 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10205201
TITLE: Bovine colostrum is a health food supplement which prevents
NSAID induced gut damage.
AUTHOR: Playford R J; Floyd D N; Macdonald C E; Calnan D P;
Adenekan R O; Johnson W; Goodlad R A; Marchbank T
CORPORATE SOURCE: University Division of Gastroenterology, Leicester General
Hospital, Gwendolen Road, Leicester LE5 4PW, UK.
(United Kingdom Wellcome Trust)
CONTRACT NUMBER: Gut, (1999 May) Vol. 44, No. 5, pp. 653-8.
SOURCE: Journal code: 2985108R. ISSN: 0017-5749. L-ISSN: 0017-5749.
Report No.: NLM-PMC1727496.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 18 Jun 1999
Last Updated on STN: 18 Jun 1999
Entered Medline: 10 Jun 1999

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record
MEDLINE REFERENCE COUNT: 23 There are 23 cited references available in
MEDLINE for this document.

AB BACKGROUND: Non-steroidal anti-inflammatory drugs (NSAIDs) are effective for arthritis but cause gastrointestinal injury. Bovine colostrum is a rich source of growth factors and is marketed as a health food supplement.

AIMS: To examine whether spray dried, defatted colostrum or milk preparations could reduce gastrointestinal injury caused by indomethacin.

METHODS: Effects of test solutions, administered orally, were examined using an indomethacin restraint rat model of gastric damage and an indomethacin mouse model of small intestinal injury. Effects on migration of the human colonic carcinoma cell line HT-29 and rat small intestinal cell line RIE-1 were assessed using a wounded monolayer assay system (used as an in vitro model of wound repair) and effects on proliferation determined using [3H]thymidine incorporation.

RESULTS: Pretreatment with 0.5 or 1 ml colostrum preparation reduced gastric injury by 30% and 60% respectively in rats. A milk preparation was much less efficacious. Recombinant transforming growth factor beta added at a dose similar to that found in the colostrum preparation (12.5 ng/rat), reduced injury by about 60%. Addition of colostrum to drinking water (10% vol/vol) prevented villus shortening in the mouse model of small intestinal injury. Addition of milk preparation was ineffective. Colostrum increased proliferation and cell migration of RIE-1 and HT-29 cells. These effects were mainly due to constituents of the colostrum with molecular weights greater than 30 kDa.

CONCLUSIONS: Bovine colostrum could provide a novel, inexpensive approach for the prevention and treatment of the injurious effects of NSAIDs on the gut and may also be of value for the treatment of other ulcerative conditions of the bowel.

L7 ANSWER 95 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1999447050 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10519561
TITLE: Biological activity of *Melaleuca alternifolia* (Tea Tree) oil component, terpinen-4-ol, in human myelocytic cell line HL-60.
AUTHOR: Budhiraja S S; Cullum M E; Sioutis S S; Evangelista L; Habanova S T
CORPORATE SOURCE: Department of Research, National College of Chiropractic, Lombard, Ill, USA.
SOURCE: Journal of manipulative and physiological therapeutics, (1999 Sep) Vol. 22, No. 7, pp. 447-53.
JOURNAL CODE: 7807107. ISSN: 0161-4754. L-ISSN: 0161-4754.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 23 Nov 1999
AB BACKGROUND: Tea tree oil is an aboriginal Australian traditional medicine for bruises, insect bites, and skin infections. It was rediscovered in the 1920s as a topical antiseptic that is more effective than Phenol. Previous studies have demonstrated its antiseptic qualities, but its effects on human white blood cells have never been investigated.

OBJECTIVE: To test the hypothesis that tea tree oil exerts its antiseptic

action through white blood cell activation.

METHODS: Crude oil and the purified "active" component were studied by using a model system that responds to bioactive components by induction of differentiation in white blood cells. Methods used included white blood cell oxidative burst assay (nitroblue tetrazolium [NBT] dye reduction); cell proliferation assay (tritiated thymidine incorporation); cell surface differentiation marker assay (flow cytometric quantitation of phycoerythrin-anti-CD 11b binding); cell viability assay (trypan blue exclusion); and cellular differentiation enzyme assay (white cell esterase staining).

RESULTS: Collectively, five assays that measure differentiation in white blood cells indicated monocytic differentiation after treatment with either crude oil or the purified active component. Both the crude oil and the purified active component, (+/-) terpinene-4-ol, caused a similar type and amount of differentiation. The culture of cells in medium containing serum caused more activation than in medium containing no serum.

CONCLUSION: The antiseptic activity of tea tree oil appears to be due, in part, to white blood cell activation.

L7 ANSWER 96 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1999435192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10507358
TITLE: Evaluation of canine lymphocyte proliferation:
comparison of three different colorimetric methods
with the 3H-thymidine incorporation
assay.
AUTHOR: Wagner U; Burkhardt E; Failing K
CORPORATE SOURCE: Institut fur Veterinar-Pathologie,
Justus-Liebig-Universitat, Giessen, Germany.
SOURCE: Veterinary immunology and immunopathology, (1999 Sep
20) Vol. 70, No. 3-4, pp. 151-9.
Journal code: 8002006. ISSN: 0165-2427. L-ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 26 Oct 1999

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB To evaluate canine lymphocyte stimulation the radioactive thymidine incorporation assay is still the method of choice. In order to find a suitable non-radioactive alternative to the standard 3H-thymidine incorporation assay, proliferation of canine peripheral blood lymphocytes (PBL) was measured with three different colorimetric assays, using the two tetrazolium salts MTT and XTT and 5-bromo-deoxyuridine (BrdU). Isolated canine PBL were stimulated with two different mitogens, Concanavalin A (Con A) and Phytohemagglutinin (PHA), using different culture conditions. Applying statistical analysis we found that BrdU and MTT showed a high correlation to the 3H-thymidine incorporation assay, although the BrdU assay proved to be more sensitive than the MTT assay. No significant correlation between the XTT assay and the radioactive method was demonstrated. Consequently, the BrdU assay is the most suitable alternative to the radioactive method.

L7 ANSWER 97 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1999027180 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9811055
 TITLE: Extracellular human T cell leukemia virus type I tax protein stimulates the proliferation of human synovial cells.
 AUTHOR: Aono H; Fujisawa K; Hasunuma T; Marriott S J; Nishioka K
 CORPORATE SOURCE: St. Marianna University School of Medicine, Kawasaki, Japan.
 SOURCE: Arthritis and rheumatism, (1998 Nov) Vol. 41, No. 11, pp. 1995-2003.
 JOURNAL CODE: 0370605. ISSN: 0004-3591. L-ISSN: 0004-3591.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
 ENTRY MONTH: 199811
 ENTRY DATE: Entered STN: 6 Jan 1999
 Last Updated on STN: 6 Jan 1999
 Entered Medline: 20 Nov 1998
 OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record
 AB OBJECTIVE: The present study was designed to investigate whether the proliferation of normal synovial cells from patients with meniscus injury is stimulated by human T cell leukemia virus type I (HTLV-I) Tax protein.

METHODS: The effect of Tax protein on the proliferation of synovial cells was evaluated using a 3H-thymidine incorporation assay. Production of cytokines was determined by enzyme-linked immunosorbent assay. Nuclear factor kappaB (NF-kappaB) DNA binding activity and the transcription of several NF-kappaB-mediated genes was detected by electrophoretic mobility shift assay and reverse transcriptase-polymerase chain reaction.

RESULTS: The proliferation of synovial cells, as well as their expression of tumor necrosis factor alpha, granulocyte-macrophage colony-stimulating factor, and interleukin-6, was significantly enhanced by extracellular Tax at concentrations of 2.5 pM to 25 nM. In contrast, extracellular bacterial extract did not change the cytokine expression or the proliferation of these cells. Proliferation of synovial cells induced by Tax protein may be due to activated expression of several cytokines and protooncogenes that contain NF-kappaB regulatory sequences.

CONCLUSION: Our results suggest that extracellular Tax can regulate the expression of endogenous cellular genes in synovial cells and may contribute to the NF-kappaB-mediated synovial hyperplasia.

L7 ANSWER 98 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1998455294 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9783973
 TITLE: Androgen responsiveness of stromal cells of the human prostate: regulation of cell proliferation and keratinocyte growth factor by androgen.
 AUTHOR: Planz B; Wang Q; Kirley S D; Lin C W; McDougal W S
 CORPORATE SOURCE: Department of Urology, Massachusetts General Hospital and Harvard Medical School, Boston 02114, USA.
 SOURCE: The Journal of urology, (1998 Nov) Vol. 160, No. 5, pp. 1850-5.
 JOURNAL CODE: 0376374. ISSN: 0022-5347. L-ISSN: 0022-5347.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 17 Nov 1998

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB PURPOSE: Growth and development of the prostate are androgen dependent and mainly influenced by stromal-epithelial interaction. It is believed that indirect androgenic activation of paracrine factors like keratinocyte growth factor (KGF) in the prostatic stroma influences the growth of epithelial cells. In this study we investigated the role androgen plays in stromal cell growth and stimulation of KGF in the human prostate.

MATERIALS AND METHODS: Stromal cells were derived from explant primary culture of human normal or benign prostatic tissue. The effect of different dihydrotestosterone (DHT) concentrations on cell proliferation was measured using 3[H]thymidine incorporation assay. The effect of DHT on levels of KGF protein was determined by Western blotting. The effect of DHT on levels of KGF gene expression was measured by various cycles of polymerase-chain-reaction (PCR) and multiplex PCR.

RESULTS: Characterization of stromal cells showed epithelial cells less than 9.5% in all passages. DHT stimulated human prostate stromal cells in a dose dependent fashion over a concentration range of 0.001-10 nM. Immunocytochemical evaluation of KGF after DHT exposure showed a higher staining intensity. Relative quantitation of Western blotting showed a 1.93-fold increase in KGF protein in the androgen treated stromal cells. At 1 nM DHT conventional and multiplex PCR revealed a significant stimulation of the KGF mRNA expression.

CONCLUSIONS: These data show for the first time that androgen stimulates cell proliferation as well as KGF protein and gene expression in human prostate stromal cells. This supports the hypothesis that androgen-induced stromal-derived KGF stimulates prostate epithelial cell growth.

L7 ANSWER 99 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998264314 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9603175
TITLE: Effect of cyclosporine and tacrolimus on the growth of Epstein-Barr virus-transformed B-cell lines.
AUTHOR: Beatty P R; Krams S M; Esquivel C O; Martinez O M
CORPORATE SOURCE: Department of Surgery, Stanford University Medical Center, California 94305, USA.
CONTRACT NUMBER: R01 AI41769 (United States NIAID NIH HHS)
SOURCE: Transplantation, (1998 May 15) Vol. 65, No. 9, pp. 1248-55.
Journal code: 0132144. ISSN: 0041-1337. L-ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal, Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 8 Jul 1998
Last Updated on STN: 8 Jul 1998
Entered Medline: 19 Jun 1998

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB BACKGROUND: Transplant patients receiving immunosuppressive drugs are at

increased risk for Epstein-Barr virus (EBV)-associated disorders including posttransplant lymphoproliferative disorder. The function of T lymphocytes, which are critical to preventing the expansion of EBV-infected B cells, is inhibited by immunosuppressive drugs. The purpose of this study was to determine whether immunosuppressive drugs have direct effects on EBV-infected B cells.

METHODS: The growth and proliferation of EBV-infected spontaneous lymphoblastoid cell lines (SLCLs), cultured in the presence or absence of cyclosporine (CsA) and tacrolimus (TAC), were measured by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and [3H] thymidine incorporation assays. The effect of CsA and TAC on the viability of SLCLs was determined by cell counts with trypan blue. Apoptosis of SLCLs was induced with an anti-Fas agonist monoclonal antibody in the presence or absence of CsA and TAC and measured by flow cytometry after terminal deoxynucleotidyl transferase end-labeling and propidium iodide staining.

RESULTS: CsA and TAC, but not sirolimus, increased the growth of SLCLs. The increased growth in the presence of CsA and TAC was attributable to enhanced cell viability and not increased cell division of SLCLs. In addition, CsA and TAC inhibited Fas-mediated apoptosis of SLCLs.

CONCLUSIONS: CsA and TAC enhance the survival of EBV-transformed B-cell lines. CsA and TAC promote or augment SLCL growth through protection from cell death but do not affect cell division. The inhibition of cell death by CsA and TAC may contribute to the expansion of EBV-infected cells in immunosuppressed individuals.

L7 ANSWER 100 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1999084858 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9869513
TITLE: Adenovirus-mediated wild-type p53 tumor suppressor gene therapy induces apoptosis and suppresses growth of human pancreatic cancer [see comments].
AUTHOR: Bouvet M; Bold R J; Lee J; Evans D B; Abbruzzese J L; Chiaio P J; McConkey D J; Chandra J; Chada S; Fang B; Roth J A
CORPORATE SOURCE: Department of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: CA 16672 (United States NCI NIH HHS)
T32-09599-08 (United States PHS HHS)
SOURCE: Annals of surgical oncology, (1998 Dec) Vol. 5, No. 8, pp. 681-8.
Journal code: 9420840. ISSN: 1068-9265. L-ISSN: 1068-9265.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 24 Mar 1999
Last Updated on STN: 12 Sep 2002
Entered Medline: 8 Mar 1999
OS.CITING REF COUNT: 9 There are 9 MEDLINE records that cite this record
AB BACKGROUND: The p53 tumor suppressor gene is mutated in up to 70% of pancreatic adenocarcinomas. We determined the effect of reintroduction of the wild-type p53 gene on proliferation and apoptosis in human pancreatic cancer cells using an adenoviral vector containing the wild-type p53 tumor suppressor gene.

METHODS: Transduction efficiencies of six p53-mutant pancreatic

cancer cell lines (AsPC-1, BxPC-3, Capan-1, CFPAC-1, MIA PaCa-2, and PANC-1) were determined using the reporter gene construct Ad5/CMV/beta-gal. Cell proliferation was monitored using a 3H-thymidine incorporation assay, Western blot analysis for p53 expression was performed, and DNA laddering and fluorescence-activated cell sorter analysis were used to assess apoptosis. p53 gene therapy was tested in vivo in a subcutaneous tumor model.

RESULTS: The cell lines varied in transduction efficiency. The MIA PaCa-2 cells had the highest transduction efficiency, with 65% of pancreatic tumor cells staining positive for beta-galactosidase (beta-gal) at a multiplicity of infection (MOI) of 50. At the same MOI, only 15% of the CFPAC-1 cells expressed the beta-gal gene. Adenovirus-mediated p53 gene transfer suppressed growth of all human pancreatic cancer cell lines in a dose-dependent manner. Western blot analysis confirmed the presence of the p53 protein product at 48 hours after infection. DNA ladders demonstrated increased chromatin degradation, and fluorescence-activated cell sorter analysis demonstrated a four-fold increase in apoptotic cells at 48 and 72 hours following infection with Ad5/CMV/p53 in the MIA PaCa-2 and PANC-1 cells. Suppression of tumor growth mediated by induction of apoptosis was observed in vivo in an established nude mouse subcutaneous tumor model following intratumoral injections of Ad5/CMV/p53.

CONCLUSIONS: Introduction of the wild-type p53 gene using an adenoviral vector in pancreatic cancer with p53 mutations induces apoptosis and inhibits cell growth. These data provide preliminary support for adenoviral mediated p53 tumor suppressor gene therapy of human pancreatic cancer.

L7 ANSWER 101 OF 188 MEDLINE on STN
ACCESSION NUMBER: 2010698115 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 20654424
TITLE: Optimization of an MCF7-E3 Cell Proliferation Assay and Effects of Environmental Pollutants and Industrial Chemicals.
AUTHOR: Desaulniers D; Leingartner K; Zacharewski T; Foster W G
CORPORATE SOURCE: Reproductive Toxicology Section, Environmental and Occupational Toxicology Division, Bureau of Chemical Hazards, Environmental Health Directorate, Health Protection Branch, Department of Health, Ottawa, Ontario, Canada, K1A 0L2.
SOURCE: Toxicology in vitro : an international journal published in association with BIBRA, (1998 Aug) Vol. 12, No. 4, pp. 409-22.
Journal code: 8712158. ISSN: 0887-2333. L-ISSN: 0887-2333.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 27 Jul 2010
Last Updated on STN: 16 Dec 2010
AB Environmental contaminants might adversely affect human health by acting as endocrine disruptors and thus need to be identified. Our objective was to optimize the MCF7 cell proliferation assay to screen industrial chemicals for potential oestrogenic effects. Growth conditions, performance of the clone E3 and WT-MCF7 cells and five methods to derive proliferation indices were compared. The E3 cells were further characterized by testing the effects of transforming growth factorbeta (TGFbeta), epidermal growth factor (EGF), insulin, testosterone, the anti-oestrogen ICI 164,384 (ICI) and environmental contaminants with known oestrogenic potential. Industrial chemicals with unknown oestrogenic effects were then tested. As expected, induction of proliferation by

estradiol-17beta (E2) was greater and less variable using the clone E3. To generate proliferation indices, the alamarBlue assay had a sensitivity comparable to that of [(3)H]thymidine incorporation ((3)H-TI). The E3 cells were not responsive to EGF (0-100 ng/ml) or insulin (0-313 ng/ml) but their proliferation was decreased (P<0.05) by TGFbeta (45 ng/ml) and testosterone (10(-8)m), which might be typical of highly oestrogen-responsive MCF7 cells. ICI (5x10(-7)m) inhibited the proliferative effects of 10(-10)m E2 and that of 10(-6)m 4-tert-octylphenol (Op) but not the proliferative effect of 10(-5)m Op, suggesting displacement of ICI by Op or induction of oestrogen-receptor independent proliferation. N-oxydiethylene-2-benzothiazole sulfenamide (OBTS) altered (3)H-TI in the MCF7 cells, although not in a dose related manner. OBTS did not induce uterotrophic effects in immature female rats, or any response in a human oestrogen chimeric receptor/reporter gene assay, suggesting that its effects were not mediated through the binding of the oestrogen-receptor. Seven other industrial chemicals were tested and had no effects. In conclusion, the MCF7 cell proliferation assay is one screening tool that permits identification of chemicals with oestrogenic potential which thus require further testing.

L7 ANSWER 102 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1998318976 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9654907
 TITLE: Effects of glucose and TGF-beta 1 on the proliferation of cultured human peritoneal mesothelial cells.
 AUTHOR: Yonekawa S
 CORPORATE SOURCE: Third Department of Internal Medicine, Kinki University School of Medicine, Osaka, Japan.
 SOURCE: Nippon Jinzo Gakkai shi, (1998 May) Vol. 40, No. 4, pp. 245-51.
 Journal code: 7505731. ISSN: 0385-2385. L-ISSN: 0385-2385.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199809
 ENTRY DATE: Entered STN: 25 Sep 1998
 Last Updated on STN: 25 Sep 1998
 Entered Medline: 15 Sep 1998

AB The exfoliation and decrease is peritoneal mesothelial cells and the presence of interstitium hyperplasia are often observed in peritoneal membrane dysfunction caused by long-term peritoneal dialysis. The suppression of peritoneal mesothelial cell proliferation may be the cause of these phenomena. The objective of this study is to clarify the mechanism by which highly concentrated glucose of peritoneal dialysis fluid inhibits mesothelial cell proliferation. We examined the effect of highly concentrated glucose in the medium on human peritoneal mesothelial cell proliferation and TGF-beta 1 mRNA expression. The effect of Ham's F12 media containing various levels of glucose concentration was compared with that of normal medium. We investigated human peritoneal mesothelial cell proliferation by [(3)H] thymidine incorporation assay and TGF-beta 1 mRNA expression on human mesothelial cells by the RT-PCR method. The suppression effect of glucose and TGF-beta 1 on human peritoneal mesothelial cell proliferation was dose-dependent (glucose; 0-5%, TGF-beta 1; 0-1000 pg/ml). TGF-beta 1 mRNA of cells in 4% glucose medium was greater than that in the control medium. The glucose-induced suppression of human peritoneal mesothelial cell proliferation was relieved by LAP and TGF-beta neutralizing antibody. In conclusion, TGF-beta 1 may play a critical role in inhibiting mesothelial cell proliferation in media with highly

concentrated glucose.

L7 ANSWER 103 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998370150 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9704522
TITLE: Comparison of 3H-thymidine incorporation
and CellTiter 96 aqueous colorimetric assays in
cell proliferation of bovine mononuclear cells.
AUTHOR: Zolnai A; Toth E B; Wilson R A; Frenyo V L
CORPORATE SOURCE: Department of Physiology and Biochemistry, University of
Veterinary Science, Budapest, Hungary.
SOURCE: Acta veterinaria Hungarica, (1998) Vol. 46, No.
2, pp. 191-7.
Journal code: 8406376. ISSN: 0236-6290. L-ISSN: 0236-6290.
PUB. COUNTRY: Hungary
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 17 Sep 1998
Last Updated on STN: 17 Sep 1998
Entered Medline: 10 Sep 1998
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB A rapid colorimetric non-radioactive assay for the determination of bovine
mitogen-induced lymphocyte proliferation in cell culture was evaluated
using a novel tetrazolium compound (MTS) and an electron coupling reagent
(PMS) provided in the CellTiter 96 kit (Promega). The results of the new
method were compared with those of the 3H-thymidine incorporation
assay using parallels obtained from the same lymphocyte population. The
concentrations used in the cell suspension of primary cultured lymphocytes
resulted in a significant signal/background ratio when cells were prepared
from peripheral blood, spleen or mesenteric lymph nodes. The same
concentrations of thymocytes resulted in a weak signal even for the
highest concentrations of mitogen. A good correlation was demonstrated
between the results of the two methods. The non-radioactive
method performed well in assays in bovine mononuclear cells
derived from prolactin-treated or -untreated calves, showing a 50% lower
responsiveness to mitogenic stimulation in prolactin-deprived animals.

L7 ANSWER 104 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998156448 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9496734
TITLE: Dipyridamole inhibits human mesangial cell proliferation.
AUTHOR: Hillis G S; Duthie L A; MacLeod A M
CORPORATE SOURCE: Department of Medicine and Therapeutics, University of
Aberdeen, UK.
SOURCE: Nephron, (1998) Vol. 78, No. 2, pp. 172-8.
Journal code: 0331777. ISSN: 0028-2766. L-ISSN: 0028-2766.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 14 May 1998
Last Updated on STN: 14 May 1998
Entered Medline: 1 May 1998
AB BACKGROUND: Many glomerular diseases are associated with mesangial cell
proliferation and the accumulation of extracellular matrix. At present,
there are, however, few treatments which can inhibit these processes. The
current study assessed the effects of the anti-platelet and putative

anti-proliferative drug dipyridamole (DP) on the growth of human mesangial cells in vitro and their production of the extracellular matrix protein, fibronectin.

METHODS: Human mesangial cell proliferation, both intrinsic and stimulated by platelet-derived growth factor, was assessed using 3H-thymidine incorporation and an MTT proliferation assay. A sandwich enzyme-linked immunosorbent assay was used to study the effects of DP on fibronectin synthesis, again in cells stimulated by transforming growth factor beta 1 and in unstimulated cells.

RESULTS: At concentrations compatible with the serum levels found in subjects consuming standard dosages, DP significantly inhibited the growth of human mesangial cells in vitro in a dose-dependent fashion. DP also abrogated the mitogenic effects of platelet-derived growth factor. It had no significant effects on the synthesis of fibronectin by these cells (either spontaneous or induced by transforming growth factor beta 1). There was no evidence of cytotoxicity.

CONCLUSION: These data suggest that DP may have a therapeutic role in proliferative glomerulonephritis and possibly other diseases characterized by cell proliferation.

L7 ANSWER 105 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998313608 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9649922
TITLE: Growth response of human coronary smooth muscle cells to angiotensin II and influence of angiotensin AT1 receptor blockade.
AUTHOR: Hafizi S; Chester A H; Allen S P; Morgan K; Yacoub M H
CORPORATE SOURCE: Department of Cardiothoracic Surgery, National Heart and Lung Institute, Imperial College School of Medicine, Harefield Hospital, Middlesex, UK.
SOURCE: Coronary artery disease, (1998) Vol. 9, No. 4, pp. 167-75.
JOURNAL CODE: 9011445. ISSN: 0954-6928. L-ISSN: 0954-6928.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 25 Sep 1998
Last Updated on STN: 25 Sep 1998
Entered Medline: 17 Sep 1998
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB BACKGROUND: The renin-angiotensin system has been implicated in the development of vascular wall thickening in cardiovascular disease, through the growth-promoting actions of the vasoconstrictive agent, angiotensin II, on vascular smooth muscle cells.

OBJECTIVE: To investigate the effect of angiotensin II on growth of human coronary artery smooth muscle cells (cSMCs) in culture, and to identify the angiotensin receptor(s) mediating such a response.

METHODS: Human cSMCs were isolated from coronary arteries of recipient hearts obtained during transplantation, and characterized by immunohistochemistry. The effect of angiotensin II on protein synthesis by cSMCs was measured by [3H]leucine incorporation and protein concentration assays. Human cSMC proliferation was assessed by [3H]thymidine incorporation assay and cell count. Reverse transcriptase polymerase chain reaction (RT-PCR) was used

to detect angiotensin receptor expression. Transient increases in intracellular calcium concentration in cSMCs in response to angiotensin II stimulation were visualized under fura-2 fluorescence microscopy.

RESULTS: Angiotensin II (1 nmol/l-10 μ mol/l) stimulated protein synthesis in cSMCs (maximum 24 \pm 2% increase in incorporation of [³H]leucine over 48 h; n = 4, P < 0.01). An increase in cellular protein content was also measured. However, angiotensin II had no effect on proliferation of quiescent cSMCs. The increased protein synthesis was completely inhibited by pretreatment with the angiotensin AT1 receptor antagonist, losartan, but not the AT2 receptor antagonist, PD123319. Expression of the angiotensin AT1 receptor subtype was detected in cSMCs by RT-PCR. Angiotensin II stimulation of cells triggered transient increases in intracellular calcium concentration, which were abolished by losartan, but were insensitive to PD123319 and pertussis toxin.

CONCLUSIONS: The results of this study in human coronary VSMCs indicate that angiotensin II and the AT1 receptor may be involved in the development of coronary artery disease in man.

L7 ANSWER 106 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998127703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9468185
TITLE: Transfer of wild-type p53 gene effectively inhibits
vascular smooth muscle cell proliferation in vitro and in
vivo.
AUTHOR: Yonemitsu Y; Kaneda Y; Tanaka S; Nakashima Y; Komori K;
Sugimachi K; Sueishi K
CORPORATE SOURCE: Department of Pathology I, Faculty of Medicine, Kyushu
University 60, Fukuoka, Japan.
SOURCE: Circulation research, (1998 Feb 9) Vol. 82, No.
2, pp. 147-56.
Journal code: 0047103. ISSN: 0009-7330. L-ISSN: 0009-7330.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19 Mar 1998
Last Updated on STN: 19 Mar 1998
Entered Medline: 12 Mar 1998
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB Wild-type p53 (wt-p53), a key protein in cell cycle regulation,
inactivates the G1 cyclins through direct activation of
p21Waf-1/Cip-1/Sdi-1. Persistent vascular smooth muscle cell (VSMC)
proliferation following vascular interventions hinders the benefits of
these therapeutics. Using the hemagglutinating virus of
Japan/liposome-mediated gene transfer method, we examined the
inhibitory effect of overexpression of exogenous wt-p53 on VSMC
proliferation in vitro and in vivo. We assessed the proliferative
activity of human p53 cDNA-transduced bovine VSMCs by DNA synthesis
assay, flow cytometry, and cell proliferation
assay. p53 gene transfer reduced thymidine
incorporation of VSMCs stimulated by platelet-derived growth
factor-BB (P<.001). The p53-transduced VSMCs underwent synthetic phase
depletion (mean, 8.02% versus 33.7% of control; P<.001) and transient G2/M
accumulation 2 days after gene transfection, and in almost all cells, G1
arrest occurred (mean, 92.6% versus 79.3% of control; P<.001) 5 days
later. The wt-p53 gene transfection also inhibited the VSMC proliferation
(P<.001) with no detectable induction of apoptosis. Cell death of
p53-transduced VSMCs was induced only by additional treatment with an

apoptosis-stimulating reagent, doxorubicin. The verification of apoptosis was made by DNA ladder, flow cytometry, and electron microscopy. In vivo transfection of p53 cDNA inhibited neointimal formation after balloon injury in rabbit carotid arteries, without apoptotic stimuli ($P < .01$). Thus, overexpression of the p53 gene in the injured arterial wall inhibits the proliferation of VSMCs in vitro and in vivo. This novel concept, including not only exogenous but also endogenous p53 overexpression in the vessel wall, may be one approach worth exploring in the treatment of patients with restenosis occurring after vascular interventions.

L7 ANSWER 107 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1998343418 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9679824
 TITLE: Cytolytic activity against allogeneic human endothelia: resistance of cytomegalovirus-infected cells and virally activated lysis of uninfected cells.
 AUTHOR: Waldman W J; Knight D A; Adams P W
 CORPORATE SOURCE: Department of Pathology, Ohio State University College of Medicine, Columbus 43210, USA. waldman.1@osu.edu
 CONTRACT NUMBER: HL56482 (United States NHLBI NIH HHS)
 SOURCE: Transplantation, (1998 Jul 15) Vol. 66, No. 1, pp. 67-77.
 Journal code: 0132144. ISSN: 0041-1337. L-ISSN: 0041-1337.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal, Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199808
 ENTRY DATE: Entered STN: 20 Aug 1998
 Last Updated on STN: 20 Aug 1998
 Entered Medline: 13 Aug 1998

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
 AB BACKGROUND: Cytomegalovirus (CMV) has been implicated as an exacerbating agent in the development of transplant vascular sclerosis; however, specific etiologic mechanisms remain unresolved. Based upon our previous observations that CMV-infected endothelial cells (ECs) stimulate proliferation and cytokine production by allogeneic T cells, we now test the hypothesis that CMV-driven cytolytic activity may contribute to graft endothelial injury.

METHODS: Limiting dilutions of CMV-seropositive or -seronegative donor-derived T cells were stimulated with CMV-infected or uninfected allogeneic ECs in the presence of interleukin-2. T-cell proliferation was monitored by assay of [3H] thymidine incorporation and stimulated T cells were tested for lytic activity against CMV-infected or uninfected radiolabeled EC targets by 51Cr release assay. Natural killer (NK) cell activity was examined by incubating freshly isolated peripheral blood mononuclear cells with 51Cr-labeled targets, followed by assay of radiolabel release.

RESULTS: CMV-infected ECs were resistant to T cell- and NK-mediated cytotoxicity regardless of donor serostatus, nature of stimulation, or level of T-cell proliferation. In contrast, although uninfected ECs were unharmed by NK cells, these targets experienced significant lysis by T cells stimulated with either uninfected or CMV-infected ECs.

CONCLUSIONS: These results implicate CMV-infected graft endothelium as a persistent source of infectious virus, a chronic stimulus for potentially destructive host inflammatory activity, and a potential trigger for the

generation of lytic injury to uninfected bystander endothelia, suggesting multiple mechanisms by which this virus might perturb equilibrium at the graft/host interface.

L7 ANSWER 108 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998114451 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9453706
TITLE: Effect of sinusoidally varying magnetic fields on cell proliferation and adenosine deaminase specific activity.
AUTHOR: Katsir G; Baram S C; Parola A H
CORPORATE SOURCE: Department of Chemistry, Ben-Gurion University of the Negev, Beer-Sheva, Israel.
SOURCE: Bioelectromagnetics, (1998) Vol. 19, No. 1, pp. 46-52.
Journal code: 8008281. ISSN: 0197-8462. L-ISSN: 0197-8462.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 6 Mar 1998
Last Updated on STN: 6 Mar 1998
Entered Medline: 26 Feb 1998
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB The effect of sinusoidally varying magnetic fields (SVMF) on chick embryo fibroblasts (CEF) was examined by two independent methods: 1) measurement of cell proliferation at 0.06-0.7 mT (100, 60 and 50 Hz) using a colorimetric assay (MTT); 2) monitoring of specific activity of adenosine deaminase (ADA) at 0.3 and 0.7 mT, 60 Hz. Both increased cell proliferation and reduced ADA specific activity are associated with cell transformation. The MTT test showed an increase in cell proliferation of up to 64% after a 24 h exposure to SVMF at 100 Hz, 0.7 mT. Cell proliferation at constant frequency (100 Hz) depended on SVMF intensity. Cell proliferation at constant intensity (0.7 mT) increased with increasing field frequency. At 0.7 mT, 60 Hz cell proliferation increased by 31%, 28%, and 26% when measured by hemocytometry, 3H-thymidine incorporation, and the MTT assay, respectively. ADA specific activity in CEF decreased by circa 48% on exposure to SVMF at 60 Hz, 0.3 mT for 24 h; only a statistically insignificant trend was seen at 0.7 mT, 60 Hz. Our findings showed that CEF cell proliferation and ADA specific activity were modified by SVMF. Both methods, independently, qualitatively detect a magnetic field effect.

L7 ANSWER 109 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998353781 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9689356
TITLE: Interferon-alpha is a potent inhibitor of basic fibroblast growth factor-stimulated cell proliferation in human uterine cells.
AUTHOR: Lee B S; Stewart E A; Sahakian M; Nowak R A
CORPORATE SOURCE: Department of Obstetrics, Gynecology and Reproductive Biology, Brigham & Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
SOURCE: American journal of reproductive immunology (New York, N.Y. : 1989), (1998 Jul) Vol. 40, No. 1, pp. 19-25.
Journal code: 8912860. ISSN: 1046-7408. L-ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 21 Oct 1998
Last Updated on STN: 21 Oct 1998
Entered Medline: 15 Oct 1998

AB PROBLEM: Abnormal uterine bleeding is a significant health problem for many women and is the number-one reason for performing hysterectomy in the United States. Leiomyomas (uterine fibroids) are benign neoplasms that are a frequent cause of abnormal uterine bleeding. The goal of this study was to assess the effects of the anti-angiogenic cytokine, interferon (INF)-alpha, on the proliferation of both leiomyoma and normal uterine cells.

METHOD OF STUDY: Primary cultures of leiomyoma, myometrial, and endometrial stromal cells were established for in vitro study. The effects of INF-alpha (10, 100, and 1000 U/ml) were tested on serum-stimulated and basic fibroblast growth factor-stimulated cell proliferation using the [3H]thymidine incorporation assay.

RESULTS: INF-alpha was a potent inhibitor of cell proliferation for all three cell types, with endometrial stromal cells showing the greatest sensitivity. The antiproliferative effect did not appear to result from toxic effects on the cells.

CONCLUSION: INFs may prove to be useful therapeutic agents for the treatment of leiomyoma-related abnormal uterine bleeding.

L7 ANSWER 110 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998088148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9426742
TITLE: Antiproliferative effects of c-myc antisense oligonucleotide in prostate cancer cells: a novel therapy in prostate cancer.
AUTHOR: Balaji K C; Koul H; Mitra S; Maramag C; Reddy P; Menon M; Malhotra R K; Laxmanan S
CORPORATE SOURCE: Department of Surgery, University of Massachusetts Medical Center, Worcester 01655, USA.
SOURCE: Urology, (1997 Dec) Vol. 50, No. 6, pp. 1007-15.
JOURNAL CODE: 0366151. ISSN: 0090-4295. L-ISSN: 0090-4295.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 17 Feb 1998
Last Updated on STN: 17 Feb 1998
Entered Medline: 3 Feb 1998

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB OBJECTIVES: To explore the possibility of using antisense oligonucleotide therapy for prostate cancer, we investigated the effect of c-myc-antisense-oligonucleotide (c-myc-As-ODN) in human prostate cancer cell lines such as LNCaP, PC3, and DU145.

METHODS: LNCaP, PC3, and DU145 cells were incubated in the presence of c-myc-As-ODN. Dose (0 to 10 microM) and time dependent (1 to 6 days) effects on proliferation and viability were examined by [3H]thymidine incorporation and MTT assay, respectively. Flow cytometry analysis was carried out to analyze cell cycle status by determining the DNA content in LNCaP cells. Control cultures received either c-myc-sense-ODN or scrambled (nonsense)

nucleotides.

RESULTS: Time- and dose-dependent decreases in DNA synthesis and cell viability were noted for all three prostate cancer cell lines after c-myc-As-ODN treatment. Further studies using LNCaP cells indicated that these changes were accompanied by an increase in the percentage of cells with less than 2N DNA content after c-myc-As-ODN treatment. The results suggest that c-myc-As-ODN induces cell death. Comparison of a c-myc-As-ODN-treated group with a group subjected to isoleucine deprivation revealed that thymidine incorporation was almost the same in c-myc-As-ODN-treated LNCaP cells and in LNCaP cells at early S phase.

CONCLUSIONS: These results suggest that c-myc-As-ODN inhibits prostate cancer cell growth and proliferation mainly by decreasing cell viability.

L7 ANSWER 111 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998019567 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9356721
TITLE: Analysis of avian lymphocyte proliferation by a new, simple, nonradioactive assay (lympho-pro).
AUTHOR: Gogal R M Jr; Ahmed S A; Larsen C T
CORPORATE SOURCE: Department of Biomedical Sciences and Pathobiology, Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg 24061, USA.
SOURCE: Avian diseases, (1997 Jul-Sep) Vol. 41, No. 3, pp. 714-25.
JOURNAL CODE: 0370617. ISSN: 0005-2086. L-ISSN: 0005-2086.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 18 Dec 1997
OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB An assessment of T-cell-mediated immune functions (i.e., lymphocyte proliferation assay) in the chicken, unlike the determination of antibody levels, is not routinely performed. This is primarily because of difficulties in the isolation of relatively pure populations of lymphocytes and the use of radioactive isotopes. To address these issues, the goals of our study were to optimize a method for isolating and enriching avian lymphocyte populations and to develop a nonradioactive lymphocyte proliferation assay. To accomplish these goals, we used a multiple slow-speed centrifugation technique combined with a "swirl" collection technique for lymphocyte isolation from chicken peripheral blood. After a fraction enriched with lymphocytes was obtained, a simple, rapid colorimetric and fluorometric assay (lympho-pro) to indirectly determine mitogen-induced proliferation was adapted and compared with the "Gold Standard" [³H]thymidine. Chickens of different ages and two genetic strains were used in this study. Lymphocytes were stimulated with various concentrations of concanavalin A (Con A, T-cell mitogen) or phorbol 12-myristate 13-acetate + ionomycin (pan lymphocyte mitogen). Our studies showed that the pattern of lymphocyte proliferation assessed by the Alamar blue-based lympho-pro assay was similar to the [³H]thymidine incorporation assay. Younger birds had higher levels of mitogen-induced proliferation when compared with adults of the same genetic strain. Because the lympho-pro assay, unlike [³H]thymidine, does not require lysis of cells to assess proliferation, cells that have undergone stimulation/proliferation can be subsequently characterized by staining with antibodies against cell surface antigens

and analysis by flow cytometry. Another notable advantage of the lympho-pro assay is the rapidity of assessment and nontoxicity. In conclusion, this assay may be of value in assessing some aspects of T-cell-mediated immunity in both avian research and avian medicine diagnostic settings.

L7 ANSWER 112 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998013283 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9352029
TITLE: Effect of rat placental culture supernatants on cellular and humoral immune responses.
AUTHOR: Malan Borel I; Menezes Freire S; Canellada A; Margni R A
CORPORATE SOURCE: Instituto de Estudios de la Inmunidad Humoral (CONICET-UBA), Facultad de Farmacia y Bioquímica de la Universidad de Buenos Aires, Argentina.
SOURCE: American journal of reproductive immunology (New York, N.Y. : 1989), (1997 Nov) Vol. 38, No. 5, pp. 366-73.
Journal code: 8912860. ISSN: 1046-7408. L-ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 22 Jan 1998
Last Updated on STN: 22 Jan 1998
Entered Medline: 6 Jan 1998

AB PROBLEM: To evaluate the effect of rat placental culture supernatants (PS) on spontaneous, mitogen- and alloantigen-induced lymphoproliferation, antibody synthesis regulation, and symmetric/asymmetric antibody ratio.

METHOD OF STUDY: The effect of PS was determined: (a) on cell proliferation of murine hybridoma cells and on spontaneous or ConA-induced proliferation of murine and rat splenocytes by thymidine incorporation; (b) on rat or mouse cell-mediated cytotoxicity (CMC) by ⁵¹Cr release; and (c) on antibody synthesis by enzyme-linked immunoadsorbent assay (ELISA).

RESULTS: With 20% PS, hybridoma cell inhibition was 37% and that of splenocytes up to 60%, whereas it was 75 and 43%, respectively, in the presence of ConA. Despite marked cell death, hybridoma proliferation index increased significantly. There was a drop in total antidinutrophenylated (DNP) immunoglobulin G1 (IgG1) antibody production and an increase in asymmetric antibody percentage, correlating with placental supernatant concentration.

CONCLUSIONS: Rat placental culture supernatants inhibit cell proliferation in all cases, diminish total antibody production, and increase the percentage of asymmetric antibodies by the hybridoma, and they increase antibody production by rat splenocytes.

L7 ANSWER 113 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1997480745 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9339390
TITLE: Glucosaminylmuramyl dipeptide (GMDP) modulates endothelial cell activities in vitro but has no effect on angiogenesis in vivo.
AUTHOR: Li C G; Kumar S; Ledger P W; Ponting J M; Carette M; Allan E
CORPORATE SOURCE: Department of Pathology and Rheumatology, Medical School, University of Manchester, UK.
CONTRACT NUMBER: (United Kingdom Wellcome Trust)

SOURCE: Inflammation research : official journal of the European Histamine Research Society ... [et al.], (1997 Sep) Vol. 46, No. 9, pp. 348-53. Journal code: 9508160. ISSN: 1023-3830. L-ISSN: 1023-3830. Switzerland

PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE)

DOCUMENT TYPE: (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 1997/11

ENTRY DATE: Entered STN: 24 Dec 1997
Last Updated on STN: 24 Dec 1997
Entered Medline: 14 Nov 1997

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB OBJECTIVE AND DESIGN: The aim of the study was to evaluate the effects of GMMP on angiogenesis in vivo and as a modulator of human umbilical vein endothelial cell proliferation, cell surface antigen expression and cell adhesion in vitro.

MATERIALS: Human umbilical vein endothelial cells (HUVEC), fertilized white leghorn chicken eggs, antibodies against adhesion molecules and glucosaminylmuramyl dipeptide (GMMP).

TREATMENT: GMMP [0.01-100 micrograms/ml] applied to cell cultures for 6-72 h and to the chick chorioallantoic membrane (CAM) for four days.

METHODS: Angiogenic activity of GMMP in vivo was assessed using the CAM assay; HUVEC proliferation was measured by tritiated thymidine incorporation and cell cycle studies; cell surface antigen expression by indirect immunofluorescence and flow cytometry; cell adhesion by quantification of [3H]-thymidine labeled leukocyte adherence to HUVEC monolayers. Statistical analysis was performed using one-way ANOVA and if necessary was followed by Duncan's multiple range test for variables.

RESULTS: GMMP induced [3H]-thymidine incorporation in a concentration- and time-dependent manner ($p < 0.003$) and significantly increased the proportion of cells in the S phase of the cell cycle ($p < 0.03$). It weakly augmented the expression of ICAM-1 and CD31 but not adhesion of leukocytes to HUVEC monolayers GMMP was not angiogenic in the CAM assay.

CONCLUSIONS: GMMP can modulate endothelial cell activity without the induction of angiogenesis in vivo which may have implications for its use as a therapeutic agent.

L7 ANSWER 114 OF 188 MEDLINE on STN

ACCESSION NUMBER: 1997141564 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8987750

TITLE: Induction of cell proliferation by fibroblast and insulin-like growth factors in pure rat inner ear epithelial cell cultures.

AUTHOR: Zheng J L; Halbig C; Gao W Q

CORPORATE SOURCE: Department of Neuroscience, Genentech, Incorporated, South San Francisco, California 94080, USA.

SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, (1997 Jan 1) Vol. 17, No. 1, pp. 216-26. Journal code: 8102140. ISSN: 0270-6474. L-ISSN: 0270-6474. United States

PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE)

DOCUMENT TYPE: English

LANGUAGE: Priority Journals; Space Life Sciences

FILE SEGMENT:

ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19 Feb 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 4 Feb 1997

OS.CITING REF COUNT: 9 There are 9 MEDLINE records that cite this record
AB Proliferation of supporting cells in the inner ear is the early major event occurring during hair cell regeneration after acoustic trauma or aminoglycoside treatment. In the present study, we examined the possible influence of 30 growth factors on the proliferation of pure rat utricular epithelial cells in culture. Utricular epithelial sheets were separated and partially dissociated from early postnatal rats via a combined enzymatic and mechanical method. The cultured utricular epithelial cells expressed exclusively epithelial cell antigens, but not fibroblast, glial, or neuronal antigens. With tritiated thymidine incorporation assays, we found that several fibroblast growth factor (FGF) family members, insulin-like growth factor-1 (IGF-1), IGF-2, transforming growth factor-alpha (TGF-alpha), and epidermal growth factor (EGF), stimulated proliferation of the utricular epithelial cells. In contrast, neurotrophins and other growth factors did not elicit any detectable mitogenic effects. Among all of the growth factors examined, FGF-2 was the most potent mitogen. When FGF-2 was added in combination with IGF-1 or TGF-alpha to the medium, combined effects were seen. These results were confirmed with BrdU immunocytochemistry. Thus, the present culture system provides a rapid and reliable assay system to screen novel growth factors involved in proliferation of mammalian inner ear supporting cells. Furthermore, immunostainings revealed that the cultured utricular epithelial cells expressed FGF and IGF-1 receptors, and utricular hair cells produced FGF-2 in vivo. The addition of neutralizing antibodies against FGF-2 or IGF-1 to the cultures significantly inhibited the utricular epithelial cell proliferation. This work suggests that FGF-2 and IGF-1 may regulate the proliferation step during hair cell development and regeneration.

L7 ANSWER 115 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1997350896 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9207272
TITLE: Mesenchymal cells stimulate human intestinal intraepithelial lymphocytes.
AUTHOR: Roberts A I; Nadler S C; Ebert E C
CORPORATE SOURCE: Department of Medicine, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick 08903, USA.
CONTRACT NUMBER: DK42166 (United States NIDDK NIH HHS)
SOURCE: Gastroenterology, (1997 Jul) Vol. 113, No. 1, pp. 144-50.
Journal code: 0374630. ISSN: 0016-5085. L-ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 5 Aug 1997
Last Updated on STN: 5 Aug 1997
Entered Medline: 23 Jul 1997

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB BACKGROUND & AIMS: Intraepithelial lymphocytes (IELs) from human intestinal mucosa proliferate minimally to T-cell stimuli. Optimal growth may depend on factors that are missing in vitro, such as accessory cells.

The aim of this study was to determine whether mesenchymal cells costimulate IELs.

METHODS: IELs were isolated from human jejunum and cultured with fibroblasts or smooth muscle cells (mesenchymal cell models for mucosal myofibroblasts) and various T-cell stimuli. Proliferation was determined by [3H]thymidine incorporation, and interleukin 2 (IL-2) production was measured by enzyme-linked immunosorbent assay. Surface molecules were detected by immunofluorescence and flow cytometry.

RESULTS: The proliferative responses of IELs to mitogen (phytohemagglutinin), superantigen (staphylococcal enterotoxin B), or anti-CD3 antibody were increased greatly by coculture with mesenchymal cells, while only slightly by peripheral-blood monocytes, the classical antigen-presenting cells. IL-2 production and receptor expression also increased. Mesenchymal cell costimulation of IEL growth required direct contact between the two cell types and was partly dependent on the integrin alpha4beta1 (very late activation 4[VLA-4]) and major histocompatibility complex (MHC) class I, as their respective antibodies blocked the effect. The surface molecules B7 (CD80), CD2, and MHC class II were not involved.

CONCLUSIONS: Optimal IEL growth depends on their contact with mesenchymal cells, an interaction that is mediated by VLA-4 and MHC class I. In mucosal immunity, basement membrane myofibroblasts likely serve this role.

L7 ANSWER 116 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1997153297 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9000587
TITLE: Flow cytometric analysis of activation markers on stimulated T cells and their correlation with cell proliferation.
AUTHOR: Caruso A; Licenziati S; Corulli M; Canaris A D; De Francesco M A; Fiorentini S; Peroni L; Fallacara F; Dima F; Balsari A; Turano A
CORPORATE SOURCE: Institute of Microbiology, University of Brescia Medical School, Italy.
SOURCE: Cytometry, (1997 Jan 1) Vol. 27, No. 1, pp. 71-6.
Journal code: 8102328. ISSN: 0196-4763. L-ISSN: 0196-4763.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 7 Apr 1997
Last Updated on STN: 7 Apr 1997
Entered Medline: 26 Mar 1997
OS.CITING REF COUNT: 21 There are 21 MEDLINE records that cite this record
AB The expression of activation antigens, namely CD25, CD69, CD71, and HLA-DR on T cells from 15 healthy individuals stimulated with different mitogens and specific antigens was evaluated by immunofluorescence assay and flow cytometric analysis and compared with cell proliferation as a function of [3H]thymidine incorporation. CD69 was the earliest expressed antigen on stimulated cells, while HLA-DR was the latest. Regardless of the stimulus used, lymphocytes expressing CD25 and CD71 were always more numerous than cells expressing CD69 and HLA-DR. Variations in the proportion of CD4+ and CD8+ T cells expressing each activation marker were observed with different antigenic stimuli. The expression of each activation marker showed overall agreement with the [3H]thymidine incorporation assay in discriminating between positive and

negative immune response. However, no correlation was observed between the percentage of CD25-, CD69-, CD71-, and HLA-DR-positive T cells and the amount of [3H]thymidine incorporation. Moreover, low doses of mitogens and antigens as well as short time of stimulation were sufficient to induce T cells to express activation antigens but not to proliferate. Our data show that results obtained by flow cytometry and [3H]thymidine incorporation may differ qualitatively, at least under certain conditions; this suggests that the 2 assays are complementary, and when combined, may give a clearer understanding of events leading to efficient cell-mediated immune response.

L7 ANSWER 117 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1998161688 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9502582
TITLE: A dye-based lymphocyte proliferation assay that permits multiple immunological analyses: mRNA, cytogenetic, apoptosis, and immunophenotyping studies.
AUTHOR: Zhi-Jun Y; Sriranganathan N; Vaught T; Arastu S K; Ahmed S A
CORPORATE SOURCE: Center for Molecular Medicine and Infectious Diseases, Department of Biomedical Sciences and Pathobiology, Virginia Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University (Virginia Te.)
CONTRACT NUMBER: 1R01-ES08043-01 (United States NIEHS NIH HHS)
SOURCE: Journal of immunological methods, (1997 Dec 15) Vol. 210, No. 1, pp. 25-39.
JOURNAL CODE: 1305440. ISSN: 0022-1759. L-ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 26 Mar 1998
Last Updated on STN: 26 Mar 1998
Entered Medline: 18 Mar 1998
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB Alamar Blue in the microenvironment of activated cells, undergoes color change and also becomes fluorescent. By using the Alamar Blue dye, we have reported a non-radioactive colorimetric assay to indirectly determine proliferation of murine lymphocytes. We further show that the pattern of mitogen-induced proliferation assessed fluorometrically was comparable to the 3H-thymidine incorporation assay (3H-Tdr assay). Of practical importance is that the color/fluorescence changes were stable at 4 degrees C in the dark for 3-4 weeks. In immunological studies, it is important to further analyze lymphocytes that have undergone activation and/or proliferation. This is not possible with the standard 3H-Tdr assay, which requires lysis of cells. In contrast, the Alamar Blue-based non-radioactive assay does not require cell lysis. We therefore tested the hypothesis that further analysis of lymphocytes is possible, after assessing the proliferation using Alamar Blue. Following assessment of proliferation in a 72-h culture, the Alamar Blue dye was washed-off and cells were re-utilized to perform additional immunological analysis. Short-term exposure of lymphocytes to Alamar Blue was not detrimental to lymphocytes, as assessed by trypan blue exclusion and the propidium iodide (PI) assays. Exposure of dexamethasone-treated cells to Alamar Blue did not interfere with the performance of apoptosis assays, such as flow cytometric analysis of PI-stained cells and microscopic examination of ethidium bromide/acridine orange-stained cells. In addition, prior exposure of lymphocytes to

Alamar Blue did not affect the analysis of chromosomal aberrations or the visualization of cell surface antigens by flow cytometry. Further, the expression of cytokine mRNA in lymphocytes previously exposed to Alamar Blue was similar to unexposed cells. Together, a notable advantage of this assay is that it now enables the investigator to maximize information by following or correlating proliferation with other immunologic events in the same cells.

L7 ANSWER 118 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1997068065 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8911393
TITLE: Decreased 3H-thymidine incorporation by human bladder epithelial cells following exposure to urine from interstitial cystitis patients.
AUTHOR: Keay S; Zhang C O; Trifillis A L; Hise M K; Hebel J R; Jacobs S C; Warren J W
CORPORATE SOURCE: Department of Medicine, Department of Veterans Affairs Medical Center, Baltimore, Maryland 21201, USA.
CONTRACT NUMBER: R01 DK44818 (United States NIDDK NIH HHS)
SOURCE: The Journal of urology, (1996 Dec) Vol. 156, No. 6, pp. 2073-8.
Journal code: 0376374. ISSN: 0022-5347. L-ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 16 Dec 1996
OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record
AB PURPOSE: Interstitial cystitis (IC) is a chronic bladder disease of unknown etiology. We sought to determine whether a cytotoxin is present in the urine of IC patients that could cause the epithelial damage seen in this disease.

MATERIALS AND METHODS: Evidence for a cytotoxin was sought using both a neutral red uptake viability assay in T24 bladder epithelial cells, and a 3H-thymidine incorporation assay in primary normal adult bladder epithelial cells and FHS 738 Bl human fetal bladder cells.

RESULTS: The neutral red assay in T24 cells indicated the presence of a cytotoxin in 2 of 9 IC patient urine specimens. However, the more sensitive assay of cell proliferation (3H-thymidine incorporation) in normal adult human bladder epithelial cells revealed antiproliferative activity in urine from 10 of 13 (77%) IC patients vs. 3 of 19 (16%) controls (two-way analysis of variance, $p = .019$). The antiproliferative activity of IC urine specimens was confirmed using FHS 738 Bl human fetal bladder cells. The antiproliferative urinary substance(s) appeared to be a low molecular weight ($< 10,000$ Da), heat stable, trypsin-sensitive factor(s).

CONCLUSIONS: Because a denuded or damaged bladder epithelium is a central finding in IC, it is possible that the antiproliferative protein(s) contributes to the pathogenesis of this disease.

L7 ANSWER 119 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1997053995 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8898374
TITLE: Aspirin-triggered lipoxins (15-epi-LX) are generated by the human lung adenocarcinoma cell line (A549)-neutrophil

interactions and are potent inhibitors of cell proliferation.

AUTHOR: Claria J; Lee M H; Serhan C N
 CORPORATE SOURCE: Department of Anesthesia, Brigham and Women's Hospital, Boston, MA 02115, USA.
 CONTRACT NUMBER: GM38765 (United States NIGMS NIH HHS)
 P01-DK50305 (United States NIDDK NIH HHS)
 SOURCE: Molecular medicine (Cambridge, Mass.), (1996 Sep) Vol. 2, No. 5, pp. 583-96.
 Journal code: 9501023. ISSN: 1076-1551. L-ISSN: 1076-1551. Report No.: NLM-PMC2230193.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199702
 ENTRY DATE: Entered STN: 27 Feb 1997
 Last Updated on STN: 27 Feb 1997
 Entered Medline: 7 Feb 1997

OS.CITING REF COUNT: 9 There are 9 MEDLINE records that cite this record
 MEDLINE REFERENCE COUNT: 30 There are 30 cited references available in MEDLINE for this document.

AB BACKGROUND: The mechanism by which aspirin (ASA) acts to protect against human cancer is not yet known. We recently showed that ASA triggers the formation of a new series of potent bioactive eicosanoids, 15-epi-lipoxins (15-epi-LXs or ASA-triggered LX [ATL]), during interactions between prostaglandin endoperoxide synthase-2 (PGHS-2) in endothelial cells and 5-lipoxygenase (LO) in leukocytes. Here, we investigated the transcellular biosynthesis of these eicosanoids during costimulation of the human tumor A549 cell line (alveolar type II epithelial cells) and neutrophils, and evaluated their impact on cell proliferation.

MATERIALS AND METHODS: A549 cells and isolated neutrophils were coincubated and mRNA expression levels of key enzymes in eicosanoid biosynthesis were measured. In addition, product formation was analysed by physical methods. The effect of LX on cell proliferation was determined by using a soluble microculture tetrazolium (MTT) assay and by measuring [3H]-thymidine incorporation.

RESULTS: Interleukin-1 beta (IL-1 beta)-primed A549 cells showed selective elevation in the levels of PGHS-2 mRNA and generated 15-hydroxyeicosatetraenoic acid (15-HETE). ASA markedly increased 15-HETE formation by A549 cells, while treatment with an inhibitor of cytochrome P450 reduced by approximately 50%, implicating both PGHS-2- and cytochrome P450-initiated routes in 15-HETE biosynthesis in these cells. Maximal production of 15-HETE from endogenous sources occurred within 24 hr of cytokine (IL-1 beta) exposure and declined thereafter. Chiral analysis revealed that approximately 85% of ASA-triggered epithelial-derived 15-HETE carries its carbon 15 alcohol group in the R configuration. Costimulation of ASA-treated A549 cells and polymorphonuclear neutrophilic leukocytes (PMN) led to production of both LXA4 and LXB4, as well as 15-epi-LXA4 and 15-epi-LXB4 (9.5 +/- 0.5 ng LX/10(7) A549 cells). 15-epi-LXA4 accounted for approximately 88% of the total amount of LXA4 produced. In addition to LXs, stimulation of A549 cells and PMN also liberated substantial amounts (77.2 +/- 8.2 ng/10(7) A549 cells) of peptidoleukotrienes (pLTs), which were not generated by either cell type alone. Addition of ASA to these co-incubations led to an increase in the amounts of LXs generated that was paralleled by a decrease in pLTs. LXA4,

LXB4, 15-epi-LXA4 and 15-epi-LXB4, as well as dexamethasone, inhibited cell proliferation at 100 nM range with a rank order of activity of 15-epi-LXB4 >>> LXB4 > dexamethasone > or = 15-epi-LXA4 > LXA4.

CONCLUSIONS: These results indicate that ASA promotes the formation of antiproliferative 15-epi-LXs by epithelial cell-leukocyte interactions. Moreover, they suggest that these novel eicosanoids, when generated within the microenvironment of tissues, may contribute to ASA's therapeutic role in decreasing the risk of human cancer.

L7 ANSWER 120 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1996176523 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8595950
TITLE: Gangliosides of migrating and nonmigrating corneal epithelium in organ and cell culture.
AUTHOR: Yang Z; Zhao Z; Panjwani N
CORPORATE SOURCE: New England Eye Center, Boston, MA 02111, USA.
CONTRACT NUMBER: EY07088 (United States NEI NIH HHS)
EY09349 (United States NEI NIH HHS)
SOURCE: Investigative ophthalmology
& visual science, (1996
Mar) Vol. 37, No. 4, pp. 501-10.
Journal code: 7703701. ISSN: 0146-0404. L-ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal, Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199604
ENTRY DATE: Entered STN: 24 Apr 1996
Last Updated on STN: 24 Apr 1996
Entered Medline: 16 Apr 1996
AB PURPOSE: To identify major gangliosides - the sialated glycolipids - of corneal epithelium; to determine which specific gangliosides, if any, are synthesized in a higher amount or are downregulated during corneal epithelial cell migration; and to determine what role, if any, they play in the modulation of corneal epithelial cell proliferation.

METHODS: [3H]-galactose-labeled and unlabeled glycolipids of migrating and nonmigrating rabbit corneal epithelium in cell and/or in organ culture were chromatographed on DEAE Sephadex to isolate gangliosides. The gangliosides eluted from the ion-exchange column were further characterized by thin-layer chromatography (TLC), glycosidase digestions, and TLC-immunostain analysis. A [3H]-thymidine incorporation assay was used to determine the effect of exogenous gangliosides on corneal epithelium cell proliferation.

RESULTS: Upon TLC of the acidic fraction eluted from the DEAE column, only two radiolabeled glycolipids (GL1 and GL2), migrating as a doublet, were detected. Regardless of whether the epithelia were prepared by cell culture or organ culture, both GL1 and GL2 were present in a significantly higher amount in migrating compared to nonmigrating epithelia. Further characterization of GL1 and GL2 identified them as gangliosides known as GM3. TLC-immunostain analysis, as well as orcinol staining of thin-layer chromatograms of gangliosides of unlabeled cells, revealed that GM3 also accumulates in a higher amount in migrating compared to nonmigrating epithelial cell cultures. Exogenous addition of GM3, but not various other gangliosides, inhibited corneal epithelial cell proliferation in a dose-dependent manner.

CONCLUSIONS: GM3 is the major ganglioside present in corneal epithelium, and its levels are elevated during corneal epithelial cell migration. It

is suggested that the ganglioside plays a role in events that modulate corneal epithelial cell proliferation.

L7 ANSWER 121 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1996314093 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8724037
TITLE: Pentoxifylline inhibits acute HIV-1 replication in human T cells by a mechanism not involving inhibition of tumour necrosis factor synthesis or nuclear factor-kappa B activation.
AUTHOR: Navarro J; Punzon M C; Pizarro A; Fernandez-Cruz E; Fresno M; Munoz-Fernandez M A
CORPORATE SOURCE: Department of Immunology, Gregorio Maranon University Hospital, Universidad Autonoma de Madrid, Spain.
SOURCE: AIDS (London, England), (1996 May) Vol. 10, No. 5, pp. 469-75.
JOURNAL CODE: 8710219. ISSN: 0269-9370. L-ISSN: 0269-9370.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 22 Oct 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 4 Oct 1996

OS.CITING REF COUNT: 6 There are 6 MEDLINE records that cite this record
AB OBJECTIVE AND DESIGN: To study the in vitro activity of pentoxifylline (PTX), which may be of benefit in AIDS, on cell proliferation, tumour necrosis factor (TNF)-alpha, interferon (IFN)-gamma (a type 1 cytokine) and interleukin (IL)-10 (a type 2 cytokine) production, viral replication and CD4+ depletion in acutely HIV-1-infected human T cells.

METHODS: T cells were stimulated with anti-CD3 antibody or phytohaemagglutinin (PHA) and infected with HIV-1 in presence or absence of PTX. Cell proliferation, CD4+ cell number, nuclear factor (NF)-kappa B activation, p24 antigen release or lymphokine content of the supernatants were evaluated by [3H]-thymidine incorporation, cytofluorimetry, electrophoretic mobility shift assays and specific enzyme-linked immunosorbent assay, respectively.

RESULTS: In HIV-1-infected T cells, PTX inhibited cell proliferation and p24 release and prevented CD4+ depletion associated with HIV replication. Moreover, PTX reduced TNF-alpha, IFN-gamma and IL-10 production and NF-kappa B activation. PTX inhibited with similar potency IFN-gamma, TNF-alpha and cell proliferation. However, the inhibition of p24 release and specially of IL-10 production required significantly lower doses of PTX. Exogenous addition of IL-2 or TNF-alpha in presence of PTX restore T-cell proliferation and NF-kappa B activation respectively, but did not affect p24 inhibition.

CONCLUSIONS: Our data suggest that the inhibitory effect of PTX on HIV replication cannot be satisfactorily explained by the inhibition of NF-kappa B or TNF-alpha. Moreover, PTX cannot be primarily considered as a TNF-alpha inhibitor and has several immunomodulatory and antiviral properties which could be of benefit against HIV-1 at various levels.

L7 ANSWER 122 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1995339334 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7542171
TITLE: Autocrine growth of transitional cell carcinoma of the

bladder induced by granulocyte-colony stimulating factor.
 AUTHOR: Tachibana M; Miyakawa A; Tazaki H; Nakamura K; Kubo A; Hata J; Nishi T; Amano Y
 CORPORATE SOURCE: Department of Urology, School of Medicine, Keio University, Tokyo, Japan.
 SOURCE: Cancer research, (1995 Aug 1) Vol. 55, No. 15, pp. 3438-43.
 Journal code: 2984705R. ISSN: 0008-5472. L-ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199508
 ENTRY DATE: Entered STN: 5 Sep 1995
 Last Updated on STN: 3 Feb 1997
 Entered Medline: 22 Aug 1995

OS.CITING REF COUNT: 8 There are 8 MEDLINE records that cite this record
 AB Granulocyte-colony stimulating factor (G-CSF) produced by nonhematopoietic malignant cells has been reported to be capable of inducing a leukemoid reaction in the host through intense stimulation of leukocyte production. Furthermore, this is frequently associated with aggressive tumor cell growth and a detrimental clinical outcome. In this study, we identified bladder cancer cells producing G-CSF with the expression of the functional receptor, which provides direct evidence of autocrine growth of bladder cancer cells induced by G-CSF. The cancer cells used in this study were obtained from a 76-year-old man who had a metastatic transitional cell carcinoma of the bladder and who demonstrated marked leukocytosis, his peripheral blood leukocyte count was 94,900 leukocytes/mm3, and his serum G-CSF level was 103 pg/ml. The culture medium in which the cancer cells were grown exclusively contained a significant amount of G-CSF (5560 pg/ml). Significant G-CSF mRNA expression and G-CSF receptor mRNA expression in the cultured cells were demonstrated by the reverse transcription-PCR method. In addition, binding studies with the use of radiolabeled recombinant G-CSF demonstrated the presence of high-affinity G-CSF binding receptors on the cultured cancer cells. Finally, the proliferation of the cultured cancer cells was stimulated by exogenous G-CSF administration, and this stimulation was inhibited by adding anti-G-CSF antibody, as demonstrated by both the flow cytometric bromodeoxyuridine incorporation technique and the [3H] thymidine incorporation assay. These results strongly suggest that G-CSF production by the bladder cancer cells studied augments autocrine growth. Therefore, we recommend exercising caution in the clinical use of G-CSF for bladder cancer patients.

L7 ANSWER 123 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1996095052 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7499084
 TITLE: ETB and epidermal growth factor receptor stimulation of wound closure in bovine corneal epithelial cells.
 AUTHOR: Tao W; Liou G I; Wu X; Abney T O; Reinach P S
 CORPORATE SOURCE: Division of Neoplastic Diseases, Mount Sinai Medical Center, New York, NY 10029, USA.
 CONTRACT NUMBER: EY04795 (United States NEI NIH HHS)
 SOURCE: Investigative ophthalmology
 & visual science, (1995 Dec) Vol. 36, No. 13, pp. 2614-22.
 Journal code: 7703701. ISSN: 0146-0404. L-ISSN: 0146-0404.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 17 Feb 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 16 Jan 1996

OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
AB PURPOSE: To determine if there is a heterogeneous pattern of endothelin (ET) receptor subtype (i.e., ETA and ETB) gene expression in the bovine corneal epithelium (BCE). To determine if ET receptor subtype stimulation increases the effectiveness of epidermal growth factor (EGF) to accelerate wound closure in a primary culture of bovine corneal epithelial cells (BCEC).

METHODS: In situ hybridization histochemistry was used to characterize ETA and ETB gene expression in the BCE. A wound closure assay evaluated wound healing rates in BCEC after 4 to 7 days in culture. [3H] thymidine incorporation and MTT assay measured proliferation.

RESULTS: ETA gene expression was appreciably higher in the basal cells than in the suprabasal cells, whereas the pattern for ETB was reversed. Epidermal growth factor (5 ng/ml) maximally increased wound closure by 145% above the control. With 5 ng/ml EGF, either 10(-9) M ET-1 or 10(-8) M sarafotoxin-6-c (s-6-c) increased wound closure by an additional 39% (P < 0.001) above that measured with 5 ng/ml EGF alone. BQ123 (10(-7) M) did not alter any of these effects of ET-1 or s-6-c. Epidermal growth factor stimulated wound closure through a selective increase in proliferation. Neither ET-1 nor s-6-c alone had any effect on proliferation or migration.

CONCLUSIONS: Both ETA and ETB genes are expressed in BCE. However, in BCEC only, ETB stimulation increases the effectiveness of EGF to stimulate wound closure. This response was caused by an increase in cell migration rather than proliferation because, after treatment with mitomycin C, neither ET-1 nor EGF stimulated wound closure.

L7 ANSWER 124 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1995399850 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7670164
TITLE: Quantitation of fibroblast population growth rate in situ using computerized image analysis.
AUTHOR: Perricone M A; Saldade V; Hyde D M
CORPORATE SOURCE: Department of Veterinary Anatomy and Cell Biology, School of Veterinary Medicine, University of California, Davis 95616, USA.
SOURCE: Microscopy research and technique, (1995 Jun 15) Vol. 31, No. 3, pp. 257-64. Journal code: 9203012. ISSN: 1059-910X. L-ISSN: 1059-910X. United States
PUB. COUNTRY: (COMPARATIVE STUDY)
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 26 Oct 1995
Last Updated on STN: 26 Oct 1995
Entered Medline: 13 Oct 1995

AB The development of computer-assisted image analysis has provided the technology to rapidly determine the population size of cultured cell monolayers in situ. We have adapted this technology to determine the population growth rate of cultured fibroblasts for use in a high-replicate format. Human lung fibroblasts were seeded into 1/2 A 96-well plates that

had one-half the culture area of standard 96-well plates. The cells were cultured in medium supplemented with different concentrations of FBS and on days 0, 1, 2, 3, 5, and 7, and their nuclei were stained with propidium iodide. A microscopic field representing one-quarter of a well of fluorescent nuclear images was captured onto a Macintosh computer, and the number of nuclei were counted using an image analysis software program. There were no significant differences between the number of nuclei counted manually and the number counted using computer-assisted software, until day 7 where the cells were multilayered ($P < 0.05$). This image analysis method was compared to other assays typically used to estimate cell proliferation or population size, namely hemocytometer counting, a rapid colorimetric staining assay using naphthol blue-black, and [3H]-thymidine incorporation. The growth rates derived using image analysis were in close agreement with results derived from hemocytometer counts and [3H]-thymidine incorporation. However, the growth rates of cells grown in high concentrations of FBS as determined using naphthol blue-black were substantially lower than results from image analysis. We conclude that this adaptation of computer-assisted image analysis provides a method to derive accurate growth curves by directly counting the number of cells in a large number of replicates.

L7 ANSWER 125 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1995230436 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7714668
 TITLE: Quantification of mitogen induced human lymphocyte proliferation: comparison of alamarBlue assay to 3H-thymidine incorporation assay.
 AUTHOR: de Fries R; Mitsuhashi M
 CORPORATE SOURCE: Medical Sciences Division, Hitachi Chemical Research Center, Inc., Irvine, California 92715, USA.
 SOURCE: Journal of clinical laboratory analysis, (1995) Vol. 9, No. 2, pp. 89-95.
 Journal code: 8801384. ISSN: 0887-8013. L-ISSN: 0887-8013.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (COMPARATIVE STUDY)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199505
 ENTRY DATE: Entered STN: 24 May 1995
 Last Updated on STN: 24 May 1995
 Entered Medline: 18 May 1995
 OS.CITING REF COUNT: 3 There are 3 MEDLINE records that cite this record
 AB Proliferation of human lymphocytes in response to various stimuli has traditionally been assessed by measuring uptake of radiolabeled nucleotides such as 3H-thymidine. We have evaluated a fluorometric assay, which uses the commercially available reagent, alamarBlue, as a potential substitute for the 3H-thymidine assay in measuring proliferation of human lymphocytes. In this assay, alamarBlue is added to a population of cells where it is reduced by mitochondrial enzyme activity. The reduced form of the reagent is fluorescent and can be quantitatively detected. The safety and convenience of the alamarBlue assay make it very attractive for use in the clinical laboratory. In this study peripheral blood mononuclear cells (PBMC) from healthy donors were stimulated using the mitogen Concanavalin A, and proliferation was assessed using either the 3H-thymidine or the alamarBlue assay. The alamarBlue assay reliably detects human PBMC and we found that the linear range of detection was 10(4) cells/well (96-well plate) to 5 x 10(5) cells/well. Detection of human PBMC is highly reproducible and the alamarBlue assay may be suitable in a number of applications where detection or relative quantitation of human PBMC is

required. The alamarBlue assay also detected mitogen induced proliferation of PBMC although with a significantly lower level of sensitivity than the standard 3H-thymidine assay.

L7 ANSWER 126 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1995354776 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7628550
TITLE: Pretreatment with oleic acid accelerates the entrance into the mitotic cycle of EGF-stimulated fibroblasts.
AUTHOR: Zugaza J L; Casabiell X A; Bokser L; Eiras A; Beiras A; Casanueva F F
CORPORATE SOURCE: Department of Medicine, Faculty of Medicine, Santiago de Compostela, Spain.
SOURCE: Experimental cell research, (1995 Jul) Vol. 219, No. 1, pp. 54-63.
JOURNAL CODE: 0373226. ISSN: 0014-4827. L-ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 21 Sep 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 1 Sep 1995

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record
AB We have previously demonstrated that pretreatment of several cell lines with cis-unsaturated fatty acids, like oleic acid, blocks epidermal growth factor (EGF)-induced early ionic signals, and in particular the [Ca²⁺]_i rise. In the present work we show that this blockade does not alter EGF-stimulated cellular proliferation evaluated by direct cell counting, but induces a powerful enhancement in the pulsed thymidine incorporation assay. The lack of effect of oleic acid on EGF-stimulated cellular proliferation was confirmed by repeated cell counts, cumulative thymidine incorporation, and protein synthesis, but a clear synergistic effect between oleic acid and EGF was again obtained by means of time course experiments with pulsed thymidine. Combined flow cytometry analysis and cell counts at earlier times in EGF-stimulated cells showed that oleic acids accelerates the entrance of cells into the replicative cycle leading to an earlier cell division. Afterward, these oleic acid-pretreated cells became delayed by an unknown compensatory mechanism in such a way that at 48 h post-EGF, the cell count in control and oleic acid-pretreated cells was equal. In conclusion (a) oleic acid accelerates or enhances the EGF mitogenic action and (b) in the long term cells compensate the initial perturbation with respect to untreated cells. As a side observation, the widely employed pulsed thymidine incorporation method as a measure of cell division could be extremely misleading unless experimental conditions are well controlled.

L7 ANSWER 127 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1994209716 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8157999
TITLE: A new rapid and simple non-radioactive assay to monitor and determine the proliferation of lymphocytes: an alternative to [3H]thymidine incorporation assay.
AUTHOR: Ahmed S A; Gogal R M Jr; Walsh J E
CORPORATE SOURCE: Department of Pathobiology, Virginia-Maryland Regional College of Veterinary Medicine (VMRCVM), Virginia Polytechnic Institute and State University

(VPI&SU),

Blacksburg 24061.
CONTRACT NUMBER: NIHCHD 20806 (United States NHLBI NIH HHS)
SOURCE: Journal of immunological methods, (1994 Apr 15)
Vol. 170, No. 2, pp. 211-24.
Journal code: 1305440. ISSN: 0022-1759. L-ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 26 May 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 13 May 1994

OS.CITING REF COUNT: 53 There are 53 MEDLINE records that cite this record
AB A one-step non-radioactive assay to determine the proliferation of murine lymphocytes, lymphoid tumor cells and hybridoma cells is described. This assay requires the addition of Alamar Blue dye to cell cultures and the degree of change in its color, which is reflective of the extent of cellular proliferation, can be determined by an ELISA plate reader. Alamar Blue must be added during the initial phase of cell culture. The pattern of concanavalin A (ConA) or anti-CD3 antibody-induced proliferative response of murine lymphocytes as assessed by Alamar Blue was similar to that of a [3H]thymidine assay. Similarly, the spontaneous proliferation curve of anti-CD3 antibody secreting cell line (YCD3-1), monocytic macrophage cell lines (PU5-1.8, P388D1, J774.1) and myeloma cells (Sp2/0) as determined by Alamar Blue closely resembled that of the [3H]thymidine assay. The minimum detectable number of proliferating cells was comparable in Alamar Blue and [3H]thymidine assays. Since cell lysis/extraction and washing procedures are not involved in the Alamar Blue assay, this approach has several distinct advantages over currently available assays (eg. [3H]thymidine). First, it allows daily monitoring of proliferation without compromising the sterility of cultures. An indication of proliferation can be evaluated (spectrophotometrically or visually) as early as 24 h after ConA stimulation. Second, unlike previously reported assays, Alamar Blue permits further analysis of proliferating cells by other methods. Analysis of cells in culture with Alamar Blue for various surface antigens (CD44, CD45RB, CD4, heat stable antigen) by flow cytometry revealed that the fluorescent profile and relative percentage of cells in cultures with the Alamar Blue were comparable to those without this reagent. The salient advantages of Alamar Blue assay over the [3H]thymidine assay include: (i) non-radioactivity; (ii) simplicity; (iii) less costly; (iv) non-labor intensive; (v) rapidity of assessment of proliferation of large number of samples; (vi) non-toxicity; (vii) usefulness in determining the kinetics of cell growth of hybridomas; and (viii) non-interference of secretion of antibodies by a hybridoma cell line.

L7 ANSWER 128 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1994273102 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8004589
TITLE: Transforming growth factor-beta inhibits proliferation of human ovarian cancer cells obtained from ascites.
AUTHOR: Hurteau J; Rodriguez G C; Whitaker R S; Shah S; Mills G; Bast R C; Berchuck A
CORPORATE SOURCE: Department of Obstetrics and Gynecology/Division of Gynecologic Oncology, Duke University Medical Center, Durham, North Carolina 27710.
CONTRACT NUMBER: CA-55640 (United States NCI NIH HHS)
SOURCE: Cancer, (1994 Jul 1) Vol. 74, No. 1, pp. 93-9.
Journal code: 0374236. ISSN: 0008-543X. L-ISSN: 0008-543X.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 29 Jul 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 18 Jul 1994

OS.CITING REF COUNT: 5 There are 5 MEDLINE records that cite this record

AB BACKGROUND: Previously, the authors found that immortalized ovarian cancer cell lines generally were resistant to the growth inhibitory effect of transforming growth factor-beta and frequently had lost the ability to produce or activate this growth factor. In this study, the authors examined whether early passage epithelial ovarian cancer cells obtained from ascites are growth-inhibited by or produce transforming growth factor-beta.

METHODS: Ovarian cancer cells were purified from ascites by percoll gradient density centrifugation, and inflammatory cells were removed using anti-CD45 antibody. The effect of transforming growth factor-beta on the proliferation of ovarian cancer cells was assessed using the thymidine incorporation assay. Immunohistochemical staining for transforming growth factor-beta 1 and beta 2 also was performed in these cells.

RESULTS: Transforming growth factor-beta (10 ng/ml) significantly inhibited [³H]thymidine incorporation in 19 of 20 (95%) primary ovarian cancers (P < 0.05). In cases in which significant inhibition was seen, the mean thymidine incorporation was 33 plus or minus 28% of control values. In addition, there was no difference in dose-dependent inhibition of proliferation between ovarian cancer cells and normal ovarian epithelial cells. Eleven of 18 ovarian cancers (61%) were found to express immunohistochemically detectable transforming growth factor-beta, but immunostaining was not observed in 39% of cases.

CONCLUSIONS: Although most primary ovarian cancer cells remain sensitive to the growth-inhibitory effect of transforming growth factor-beta, loss of production may interrupt the transforming growth factor-beta autocrine inhibitory loop and play a role in the development of some ovarian cancers.

L7 ANSWER 129 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1994315899 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7518883
TITLE: Functional glucocorticoid receptor modulates pancreatic carcinoma growth through an autocrine loop.
AUTHOR: Norman J; Franz M; Schiro R; Nicosia S; Docs J; Fabri P J; Gower W R Jr
CORPORATE SOURCE: Department of Surgery, University of South Florida College of Medicine, Tampa 33612.
SOURCE: The Journal of surgical research, (1994 Jul) Vol. 57, No. 1, pp. 33-8.
Journal code: 0376340. ISSN: 0022-4804. L-ISSN: 0022-4804.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 5 Sep 1994
Last Updated on STN: 3 Feb 1997

Entered Medline: 22 Aug 1994

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB Several peptide hormones have been shown to influence growth and function in pancreatic carcinoma and have given evidence for an autocrine feedback loop governing the proliferation of these malignant cells. Conversely, steroid hormones including glucocorticoids have been shown to inhibit the growth of pancreatic cancer cells; however, the prevalence of the glucocorticoid receptor or its mechanism of growth suppression in these tumors is unknown. The ability of growth factors thought to be active in this autocrine loop to reverse the glucocorticoid-induced growth inhibition was studied in vitro in a human pancreatic adenocarcinoma (HPAC) cell line with a well-characterized glucocorticoid receptor (GR). The glucocorticoid dexamethasone (DEX) inhibited growth in a dose-dependent manner as measured by a [3H]thymidine incorporation assay as well as an MTT cell proliferation assay. Maximal effects were seen within 48 hr at a concentration of 100 nM DEX, suppressing growth to approximately 18% of control. When the maximally suppressed DEX-treated cells were exposed to exogenous growth factors, they rapidly attained or exceeded the growth rate of control cells: insulin-like growth factor = 106%, transforming growth factor- α = 134%, insulin = 151%, and epidermal growth factor = 187% (all $P < 0.05$, Student's t test). In order to determine the frequency of the GR in pancreatic cancer and the clinical relevance of our findings, immunohistochemical staining for the GR was performed on 20 human tumors. Twelve (60%) of all cancers, as well as all normal pancreatic tissues ($n = 4$), stained positively for cytoplasmic and/or nuclear GR with expression correlating highly with degree of tumor differentiation (Kruskal-Wallis test, $P < 0.05$). (ABSTRACT TRUNCATED AT 250 WORDS)

L7 ANSWER 130 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1994062490 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8243206
TITLE: Analysis of lymphocyte activation and proliferation by video microscopy and digital imaging.
AUTHOR: Teague T K; Munn L; Zygourakis K; McIntyre B W
CORPORATE SOURCE: Department of Immunology, University of Texas M.D. Anderson Cancer Center, Houston 77030.
SOURCE: Cytometry, (1993 Oct) Vol. 14, No. 7, pp. 772-82.
Journal code: 8102328. ISSN: 0196-4763. L-ISSN: 0196-4763.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 1 Feb 1994
Last Updated on STN: 1 Feb 1994
Entered Medline: 5 Jan 1994

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB Video microscopy and digital imaging were used as a noninvasive method to quantitatively analyze lymphocyte activation and proliferation. This method takes advantage of the fact that upon activation lymphocytes blast and become significantly larger before proliferating. The mean cell sizes of T lymphocytes in an activation kinetics assay were measured by digital image analysis and compared to [3H]-thymidine incorporation of cells under the same treatment. An increase in cell size was observed before [3H]-thymidine incorporation; therefore the digital imaging assay is more sensitive in determining the earliest time-point of activation. Also, the digital imaging assay was comparable to the [3H]-thymidine incorporation assay in providing information about the

extent and rates of T lymphocyte proliferation. Cellular DNA was stained with propidium iodide to show that the larger blasting cells in the population of activated T lymphocytes were indeed the cells that accounted for the increase in DNA synthesis and thus an increase in cell size can be correlated with activation.

L7 ANSWER 131 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1993194511 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8449682
TITLE: Platelet-derived growth factor: receptor expression in corneas and effects on corneal cells.
AUTHOR: Hoppenreijds V P; Pels E; Vrensen G F; Felten P C; Treffers W F
CORPORATE SOURCE: Department of Morphology, The Netherlands Ophthalmic Research Institute, Amsterdam.
SOURCE: Investigative ophthalmology & visual science, (1993 Mar) Vol. 34, No. 3, pp. 637-49.
JOURNAL CODE: 7703701. ISSN: 0146-0404. L-ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 23 Apr 1993
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Apr 1993
OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
AB PURPOSE: Platelet-derived growth factor (PDGF), a major mitogen and chemoattractant, is a dimeric molecule of disulfide-bonded A and/or B polypeptide chains (PDGF-AA/AB/BB). Two PDGF receptors (PDGFR) exist, alpha and beta, which dimerize after ligand exposure. The alpha-receptor binds both A- and B-chains, whereas the beta-receptor preferentially binds the B-chain. Whether PDGFR are present on, and whether PDGF is mitogenic for, corneal cells was investigated.

METHODS: For receptor determination, a two-step immunoperoxidase technique with monoclonal antibodies against both alpha- and beta-receptors was applied on frozen sections of human and bovine corneas. To test the mitogenic activity of PDGF-BB, two proliferation assays, the DNA synthesis assay (3H-thymidine incorporation) and the colorimetric MTT assay, were used for cultured bovine corneal endothelial cells (BCEC) and human corneal fibroblast (HCF).

RESULTS: Both receptors were present on epithelial cells, stromal fibroblasts, and endothelial cells, the beta-receptor being most abundant. In BCEC, minimal and maximal effects on DNA synthesis occurred at 10 ng/ml and 50-100 ng/ml PDGF, respectively. For HCF, the minimal and maximal effective doses were 1 ng/ml and 25-100 ng/ml of PDGF, respectively. The MTT assay, carried out in BCEC only, showed a minimal and maximal cell activity at 1 ng/ml and 10-100 ng/ml of PDGF, respectively.

CONCLUSIONS: The presence of PDGFR in human corneal epithelium, fibroblasts, and endothelium and the mitogenic effects of PDGF on corneal cells indicate that PDGF may play a role in corneal wound healing.

L7 ANSWER 132 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1993194503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8383644
TITLE: Minoxidil inhibits ocular cell proliferation and lysyl

hydroxylase activity.
AUTHOR: Handa J T; Murad S; Jaffe G J
CORPORATE SOURCE: Department of Ophthalmology, Duke University Medical
Center, Durham, North Carolina.
CONTRACT NUMBER: AR17128 (United States NIAMS NIH HHS)
AR28304 (United States NIAMS NIH HHS)
SOURCE: Investigative ophthalmology
& visual science, (1993
Mar) Vol. 34, No. 3, pp. 567-75.
Journal code: 7703701. ISSN: 0146-0404. L-ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 23 Apr 1993
Last Updated on STN: 23 Apr 1993
Entered Medline: 12 Apr 1993

AB PURPOSE: To examine the antiproliferative and lysyl
hydroxylase-suppressing effects of minoxidil on cultured proliferating and
density-arrested human retinal pigment epithelial cells (hRPE) and Tenon's
capsule fibroblasts (hTCF).

METHODS: Proliferating and density-arrested hRPE and hTCF,
exposed to minoxidil (0.1-5 mM) for 15 min to 7 days, were examined by
proliferation assays, [3H]thymidine
incorporation, trypan-blue exclusion, and phase-contrast
microscopy. The lysyl hydroxylase-suppressing effects were examined in
confluent hRPE exposed to minoxidil (0.01-1 mM) using
L-[4,5-3H]-lysine-labeled procollagen substrate and measuring the amount
of tritium released as 3H2O after vacuum distillation.

RESULTS: Minoxidil (0.1-5 mM) inhibited the proliferation of subconfluent
cultures of hRPE and hTCF in a dose-dependent manner with a half-maximal
effect at 1.5 and 2.5 mM, respectively. The antiproliferative effect,
detectable within 24 hr, occurred with a limited exposure period and
persisted even after removal of minoxidil from the culture medium. In
contrast, 1-5 mM minoxidil had minimal effect on density-arrested hRPE and
hTCF. However, at doses above 3 mM, although minoxidil had no effect on
the number of density-arrested hRPE, morphologic and viability experiments
indicated signs of cytotoxicity. Minoxidil (0.1-1 mM) caused a maximum of
71% reduction in the activity of lysyl hydroxylase, an enzyme needed for
stable cross-links in collagen.

CONCLUSIONS: Minoxidil may be a useful drug for the treatment of
conditions such as proliferative vitreoretinopathy and bleb scarring after
trabeculectomy, disorders with unwanted cell proliferation and collagen
production.

L7 ANSWER 133 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1993143337 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8424669
TITLE: Adriamycin conjugates of human transferrin bind transferrin
receptors and kill K562 and HL60 cells.
AUTHOR: Berczi A; Barabas K; Sizensky J A; Faulk W P
CORPORATE SOURCE: Center for Reproduction and Transplantation Immunology,
Methodist Hospital of Indiana, Indianapolis 46202.
SOURCE: Archives of biochemistry and biophysics, (1993 Jan)
Vol. 300, No. 1, pp. 356-63.
Journal code: 0372430. ISSN: 0003-9861. L-ISSN: 0003-9861.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 12 Mar 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 23 Feb 1993

OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record

AB Adriamycin (ADR) was coupled to human transferrin (TRF) by using a glutaraldehyde crosslinking method. The TRF-ADR conjugates were separated by column chromatography and the molar ratio of ADR to TRF (i.e., conjugation number) for the studied conjugates was found to be 1.2. Analysis in sodium dodecyl sulfate-polyacrylamide gels demonstrated that TRF-ADR conjugates with this molar ratio had the same mobility as native TRF and contained few aggregates. The ADR remained conjugated to TRF under conditions of decreased pH known to occur in many intracellular compartments, and analysis by spectrofluorometry revealed that the conjugated ADR retained its ability to intercalate DNA. The TRF-ADR conjugates were shown by flow cytometry to preferentially bind tumor cells and cell-bound conjugates were found to be laterally mobile within plasma membranes. The binding of TRF-ADR conjugates was determined to be saturable, and competition experiments done with both radioiodinated and fluorescein-labeled TRF-ADR conjugates demonstrated dose-dependent inhibition of conjugate binding by unlabeled TRF, indicating that TRF-ADR conjugates were bound by TRF receptors. Cytotoxicity studies performed with tritiated thymidine incorporation and tetrazolium reduction assays revealed that TRF-ADR conjugates inhibited the proliferation of both K562 and HL60 cells in culture more effectively than free ADR. Such conjugates could provide a delivery system for ADR that would target the drug and possibly diminish its dose-associated complications.

L7 ANSWER 134 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1992011559 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1717445

TITLE: The increased potency of cross-linked lymphocyte function-associated antigen-3 (LFA-3) multimers is a direct consequence of changes in valency.

AUTHOR: Pepinsky R B; Chen L L; Meier W; Wallner B P
CORPORATE SOURCE: Biogen, Inc., Cambridge, Massachusetts 02142.
SOURCE: The Journal of biological chemistry, (1991 Sep 25)
Vol. 266, No. 27, pp. 18244-9.
Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 29 Jan 1996
Entered Medline: 29 Oct 1991

OS.CITING REF COUNT: 4 There are 4 MEDLINE records that cite this record

AB We have used chemically cross-linked dimers, trimers, and tetramers of lymphocyte function-associated antigen-3 (LFA-3) to study the role of multivalency in the interaction of the protein with its receptor, CD2. The cross-linked adducts showed enhanced activity in systems where LFA-3 has been shown to (i) block LFA-3/CD2 interactions in a rosetting assay and (ii) provide through the CD2 on peripheral blood lymphocytes a trigger for T-cell proliferation. The level of increase was directly related to the valency state of the multimers. In the rosetting assay, the dimers, trimers, and tetramers, by weight, exhibited 15-, 150-, and 430-fold

increases in activity over monomeric LFA-3. In the proliferation assay, the tetramer produced a 6-fold increase in thymidine incorporation at 0.06 micrograms/ml, the trimer was 100 times less active than the tetramer, and the dimer and monomer were inactive. The LFA-3 multimers were generated using a three-step cross-linking chemistry that was targeted at the carbohydrates on LFA-3. With this procedure over 60% of the starting protein was converted into multimers with no effect on function. The cross-linking approach should be applicable to other surface antigens, providing a simple method for analyzing multivalent interactions.

L7 ANSWER 135 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1992198327 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1801697
TITLE: Development of a rapid, highly sensitive, non-radioactive assay system for hematopoietic growth factors.
AUTHOR: Hintz-Obertreis P; Krumwieh D; Seiler F R
CORPORATE SOURCE: Research Laboratories of Behringwerke AG, Marburg, Germany.
SOURCE: Behring Institute Mitteilungen, (1991 Dec) No. 90, pp. 99-103.
Journal code: 0367532. ISSN: 0301-0457. L-ISSN: 0301-0457.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 9 May 1992
Entered Medline: 21 Apr 1992

AB The aim of this study was to develop non-radioactive cell line proliferation assays. The human leukemic cell line TF1 (Kitamura et al., 1989) was used for the determination of the specific biological activity of recombinant human (rhu) granulocyte-macrophage colony-stimulating factor (GM-CSF) and rhu Interleukin 3 (IL-3) by a simple and economical fluorometric assay with a sensitivity similar to the measurement of 3H-thymidine uptake. The TF1 cell line responds to rhu IL-3, rhu GM-CSF and to a lesser extent to rhu Erythropoietin (EPO) and mast cell growth factor (MGF), but not to rhu G-CSF. It is dependent upon rhu GM-CSF for survival in culture. For the proliferation assay 1×10^4 TF1 cells were incubated with 20 ng - 0.256 pg rhu GM-CSF or rhu IL-3 at 37 degrees C and 5% CO2 in humidified atmosphere. After 48 h the cells were washed twice with PBS and were incubated with 4-Methylumbelliferyl-heptanoate for 60 min. Fluorescence was determined on a Titertek Fluoroskan II (Flow Laboratory), and results were given as fluorescence units using a 355 nm excitation filter and a 480 nm emission filter. The developed assay showed an interassay variability lower than 15%. The sensitivity of the proliferation assays in the same range as the thymidine incorporation assays.

L7 ANSWER 136 OF 188 MEDLINE on STN
ACCESSION NUMBER: 1987279417 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3112053
TITLE: AIDS studies in Japan.
AUTHOR: Harada S; Yamamoto N
SOURCE: Japanese journal of cancer research : Gann, (1987 May) Vol. 78, No. 5, pp. 415-27. Ref: 88
Journal code: 8509412. ISSN: 0910-5050. L-ISSN: 0910-5050.
Report No.: RSP-061952; POP-00198952.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Population; AIDS

ENTRY MONTH: 198709

ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 10 Sep 1987

REFERENCE COUNT: 88 There are 88 cited references for this document.

AB The AIDS Surveillance System in Japan was set up in 1984 and by 1987, 29 AIDS patients had been reported. 10 were homosexuals, 16 were hemophiliacs and 3 were heterosexuals. 9 out of 16 hemophiliacs with AIDS had A-type hemophilia. 2 females were also reported as victims of AIDS. 19 patients have died 5 male homosexuals (4.4%) out of 113 (93 Japanese and 20 Foreigners) individuals were anti-HIV-positive. In 1984 sera from 65 hemophiliacs, 85 hemodialysis patients and 304 healthy volunteer blood donors were examined and 10 (15.4%) of the hemophiliacs proved to be anti-HIV positive. On the other hand, in Tokyo and Nagasaki 50-60% were positive, but in Tottori and Osaka only 25-28% were positive. The enzyme-linked immunosorbent assay (ELISA) test is widely used to detect antibodies, however, the test often gives false-positive reactions, and the blood must be reexamined by means of the Western-blot test or IF method. Therefore, a simple particle agglutination (FA) assay was developed by the authors using gelatin beads as the artificial antigen carrier. This assay is extremely sensitive as compared to IF and ELISA. Among HTLV-1/ATLV-carrying T-cell lines, all except one (TCL-As) were susceptible to HIV infection and showed cytopathic effect (CPE). HIV has quite a broad host range in vivo and in vitro. HIV was detected in brain macrophages from AIDS patients with encephalopathy. HIV may also infect nerve cells or glial cells. The MT-4 cell line was found to be most prone to HIV infection. In order to evaluate the virus-induced CPE of infected MT-4 cells, the H-thymidine incorporation method (cell proliferation assay) was developed that involved that involves measuring the survival of the cells. Inhibition of DNA synthesis in infected MT-4 cells was detected by this assay when the CPE was observed microscopically. This assay system is also useful for measuring the amount of infectious virus. Many chemico-physical agents such as suramin, antimoniotungstate (HFA-23), phosphonoformic acid, ribavirin, 3-azido-3-deoxythymidine (AZT) have suppressive effects on the replication of HIV in vitro. Glycyrrhizin administration was responsible for improvement of immune function in 6 of 7 asymptomatic HIV carriers. Prostaglandin E2 (PGE2) and 12-O-tetradecanoylphorbol-13-acetate (TPA) were found to enhance the production of HIV significantly in infected MT-4 cells. The cell proliferation assay is used for the mass screening of neutralizing antibodies whose presence in the sera from 21 patients with AIDS, 10 individuals with ARC, 20 healthy male homosexuals and 10 healthy males was examined. The assay was sensitive enough to detect neutralizing antibodies up to a dilution of 1:10 thousand. The system using MT-4 cells seems to be suited for this purpose.

L7 ANSWER 137 OF 188 MEDLINE on STN

ACCESSION NUMBER: 1988036017 MEDLINE

DOCUMENT NUMBER: PubMed ID: 3312611

TITLE: In vitro proliferation of human lymphocytes measured by an enzyme immunoassay using an anti-5-bromo-2-deoxyuridine monoclonal antibody.

AUTHOR: Martinon F; Rabian C; Loiseau P; Ternynck T; Avrameas S; Colombani J

CORPORATE SOURCE: Laboratoire d'Immunologie et d'Histocompatibilite, Hopital Saint Louis, Paris, France.

SOURCE: Journal of clinical & laboratory immunology, (1987

Jul) Vol. 23, No. 3, pp. 153-9.
 Journal code: 7808987. ISSN: 0141-2760. L-ISSN: 0141-2760.
 Italy
 PUB. COUNTRY: (COMPARATIVE STUDY)
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198711
 ENTRY DATE: Entered STN: 5 Mar 1990
 Last Updated on STN: 5 Mar 1990
 Entered Medline: 24 Nov 1987

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB A previously described, non radioactive method for the measure of in vitro mouse lymphocyte proliferation was applied to human lymphocyte proliferation assays. It involved incorporation into DNA, during cell multiplication, of 5-bromo-2-deoxyuridine (BUDR), a thymidine analogue. BUDR-DNA was then assayed by a sandwich enzyme immunoassay (BUDR-EIA) using an anti-BUDR monoclonal antibody (McAb 76-7). BUDR-DNA from crude cell extracts was first immobilized on microtitration plates coated with McAb 76-7. In a second step BUDR-DNA was reacted again with McAb 76-7 conjugated to horse radish peroxidase. The quantity of peroxidase in microtitration wells was then measured by the coloration of o-phenylenediamine (492 nm). Titration curves obtained with dilutions of crude extracts were compared to the curve obtained with a purified BUDR-DNA reference solution. Results were expressed as equivalent ng BUDR-DNA/ml. BUDR-EIA was compared to 3H-thymidine incorporating assay for the measure of lymphocyte proliferation induced by PHA mitogen, candidine and tuberculine antigens and mixed lymphocyte culture. Excellent correlation between both assays was observed for each experiments ($r = 0.953$ to 0.999). Overall correlation coefficient for the 5 experiments was 0.785 , indicating greater variation of BUDR than 3H-thymidine incorporation, according to the mitogen or antigen used and the culture conditions. This could be due to that fact that BUDR-EIA measured only BUDR incorporated into DNA, while 3H-thymidine incorporation assay measured 3H-thymidine both incorporated into DNA, and stocked into the cell before DNA incorporation. BUDR-EIA would thus reflect cell proliferation more exactly than 3H-thymidine incorporation assay. The sensitivities of both techniques were comparable. (ABSTRACT TRUNCATED AT 250 WORDS)

L7 ANSWER 138 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1985184164 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 2580921
 TITLE: Proliferation and interferon production in whole blood samples and isolated lymphocyte preparations.
 AUTHOR: Doldi K; Leroux M; Augustin R; Kirchner H; Kalden J R
 SOURCE: Journal of interferon research, (1985 Winter)
 Vol. 5, No. 1, pp. 55-64.
 Journal code: 8100396. ISSN: 0197-8357. L-ISSN: 0197-8357.
 United States
 PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE)
 DOCUMENT TYPE: English
 LANGUAGE: Priority Journals
 FILE SEGMENT: 198506
 ENTRY MONTH: Entered STN: 20 Mar 1990
 ENTRY DATE: Last Updated on STN: 6 Feb 1998
 Entered Medline: 19 Jun 1985

OS.CITING REF COUNT: 1 There are 1 MEDLINE records that cite this record

AB To establish a method for the evaluation of immunological parameters in small blood samples, a whole blood technique was developed for the estimation of mitogen induced cell proliferation and interferon

(IFN) production. The results obtained were compared with data using isolated peripheral blood lymphocytes (PBL). Mixtures of heparinized whole blood and culture medium or equal numbers of PBL of healthy volunteers or of patients were cultured with the mitogens concanavalin A, phytohemagglutinin, pokeweed mitogen or the monoclonal antibodies OKT3 and anti-Leu-4. Cell proliferation as measured by 3H-thymidine incorporation and interferon production were found to be of higher magnitude in the whole blood assay. The only situation in which results were similar was pokeweed mitogen induced cell proliferation. Since in the whole blood assay the cell populations are present in their natural distribution, this test system may reflect the in vivo situation better than the test using isolated lymphocytes. Furthermore, our data indicate that whole blood samples may be used clinically for the evaluation of different immune parameters, as data on a limited number of patients with Hodgkin's disease have shown.

L7 ANSWER 139 OF 188 MEDLINE on STN
 ACCESSION NUMBER: 1977250782 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 142787
 TITLE: Rapid multiparameter analysis of cell stimulation in mixed lymphocyte culture reactions.
 AUTHOR: Traganos F; Gorski A J; Darzynkiewicz Z; Sharpless T; Melamed M R
 SOURCE: The journal of histochemistry and cytochemistry : official journal of the Histochemistry Society, (1977 Jul) Vol. 25, No. 7, pp. 881-7. Journal code: 9815334. ISSN: 0022-1554. L-ISSN: 0022-1554. United States
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 197710
 ENTRY DATE: Entered STN: 14 Mar 1990
 Last Updated on STN: 14 Mar 1990
 Entered Medline: 28 Oct 1977
 OS.CITING REF COUNT: 2 There are 2 MEDLINE records that cite this record
 AB A flow-cytofluorometric method, based on the differential stability of deoxyribonucleic acid versus ribonucleic acid with the metachromatic dye, acridine orange, simultaneously measures the following parameters of stimulation in mixed lymphocyte cultures: (a) number of nonstimulated cells; (b) total number of stimulated lymphocytes; (c) number of stimulated lymphocytes in G1, S and G2 + M phases of the cell cycle; (d) number of macrophages; (e) number of dead cells. The progress of lymphocyte stimulation may also be measured by a parameter representing ribonucleic acid accumulation per cell. The method is rapid, avoids cell rinsing, fixation and centrifugation and is applicable to microcultures. Multiparameter analysis of cell stimulation which provides simultaneous measurements of lymphocyte proliferation and accumulation of ribonucleic acid per cell may prove to be a more sensitive assay of histocompatibility than tests based only on cell proliferation (tritiated thymidine incorporation).

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Provides More Current and Complete Information
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enhanced with thesauri for the European Patent Classifications
NEWS 4 MAY 02 MEDLINE Improvements Provide Fast and Simple Access to DOI and
Chemical Name Information
NEWS 5 MAY 12 European Patent Classification thesauri added to the INPADOC
files, PCTFULL, GBFULL and FRFULL
NEWS 6 MAY 23 Enhanced performance of STN biosequence searches
NEWS 7 JUN 20 STN on the Web Enhanced with New Patent Family Assistant and
Updated Structure Plug-In
NEWS 8 JUN 20 INPADOC databases enhanced with first page images
NEWS 9 JUN 20 PATDPA database updates to end in June 2011
NEWS 10 JUN 26 MARPAT Enhancements Save Time and Increase Usability
NEWS 11 JUL 25 STN adds Australian patent full-text database,
AUPATFULL, including the new numeric search feature.
CA Sections Added to ACS Publications Web Editions
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enhanced legal status
NEWS 14 AUG 18 Upgrade now to STN Express, Version 8.5
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Articles for More Than 100 Journal Titles
NEWS 16 SEP 01 Older Versions of STN Express to be Discontinued
Beginning in March 2012
NEWS 17 SEP 09 USAN Database Updates Offer Superior Currency on STN(R)
NEWS 18 SEP 26 STN Adds Canadian Patent Full-text Database - CANPATFULL
NEWS 19 SEP 26 GOREF and ENCOMPLIT databases were reloaded on
September 24, 2011.

NEWS 20 SEP 26 Updates to the IFIPAT/IFIUDB/IFICDB databases have resumed.
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 NEWS 22 SEP 26 Access AUPATFULL and CANPATFULL databases with STN Viewer
 NEWS 23 OCT 26 New STN Revolutionizes Patent Searching for Professionals
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 NEWS 25 DEC 1 CAS Expands Global Patent Coverage - Intellectual Property
 Corporation of Malaysia Becomes 62nd Authority on CA/CAPLUS
 NEWS 26 DEC 5 STN on the Web Enhancements Include Compatibility with
 Microsoft Windows 7
 NEWS 27 DEC 14 Removal of ITRD and PATIPC databases from STN
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=> S (vascular smooth muscle cells) (S) (Umbilical vein epithelial cell)
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 CELL)

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